



The 4th EURASIA CONGRESS OF INFECTIOUS DISEASES

01-05 JUNE 2011

HOLLYWOOD HOTEL & CONGRESS CENTER, SARAJEVO-BOSNIA & HERZEGOVINA

“Clinical Microbiology, Infectious Diseases, Immunology and Epidemiology”

EDITORS

Aysegul Karahasan
Murat Gunaydin
Sead Ahmetagic
Nijaz Tihic
Salih Hosoglu
Hakan Leblebicioglu



ABSTRACT BOOK



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Mikrobiologa
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Hercegovine



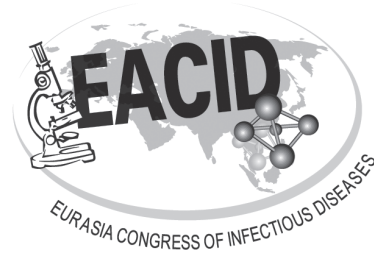
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Bukres Sokak No: 3/20 Kavaklıdere-ANKARA

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SCIENTIFIC PROGRAM

1 June, 2011

Hours

08:30-17:00

Registration

Hall A

17:00-18:30

OPENING CEREMONY

Welcome Remarks

Hakan Leblebicioglu

President of Congress

President of Blacksea Society of Clinical Microbiology and Infectious Diseases

Sead Ahmetagic

President of Congress

President of Association of Infectiologists in Bosnia and Herzegovina

The Mission of the EACID

Murat Gunaydin, Salih Hosoglu

18:30

Welcome Reception

02 June, 2011

Hall A

09:00-09:45

Plenary Lecture

Chairperson:

Dilek Arman

Hakan Leblebicioglu

Infections in Cancer Patients

Murat Akova

Hall B

09:45-10:15

COFFEE BREAK

PANEL 1

10:15-11:30

Outbreaks: From the view point of the new millennium

Chairpersons:

Aysegul Karahasan

Nijaz Tihic

Host Immune History and Cross Protection During Pandemic H1N1 Infection

David Kelvin

Crimean-Congo Hemorrhagic Fever-The Experience of Turkey

Gul Ruhsar Yilmaz

Tularemia: Laboratory Diagnosis and Molecular Epidemiology

Selcuk Kilic

Vector Borne Diseases- An Update

Zarema Obradovic

PANEL 2

Hospital Infection Control in Countries with Limited Resources

Chairpersons:

Sercan Ulusoy

Amela Dedeic Ljubovic

Hand Hygiene

Ziad Memish

Hospital Infection Control Basics

Serhat Unal

Hospital Infection Control in Bosnia

Amela Dedeic Ljubovic

Nosocomial Bloodstream Infections Surveillance-Croatian Experience

Mirjana Balen

Supported by Turkish Society of Hospital Infections and Control (HIS)

11:30-12:30

Oral Presentations-I

Chairpersons:

Mustafa Altindis

Snezana Mehanic

Roche Diagnostics Sattelite

Sabine Muench Garthoff

12:30-13:30

LUNCH

Hours
13:30-15:00

PANEL 3

Sterilization and Disinfection Practices in Healthcare Settings

Chairpersons:
Bulent Gurler
Amer Custovic

Setting Up Sterilization Units in Health Care Settings
Wim Renders

International Standards and Guidelines Related to Sterilization
Duygu Percin

Disinfection of Endoscopes
Saban Esen

Supported by Turkish Society of Disinfection Antisepsis Sterilization (DAS)

PANEL 4

Current Situation in Sexually Transmitted Diseases

Chairpersons:
Mustafa Sunbul
Mario Poljak

The Epidemiology of HIV/AIDS Infection in South Eastern European Countries
Mario Poljak

Status of Major Sexually Transmitted infections in Bosnia and Herzegovina
Sabina Mahmutovic

Bacterial STD Infections: An Update
Sibel Gundes

15:00-15:30

COFFEE BREAK

15:30-17:00

PANEL 5

Urinary Tract Infections

Chairpersons:
Gaye Usluer
Selma Uzunovic-Kamberovic

Epidemiology of Urinary Tract Infections
Ibrahim Cağatay Acuner

The Role of Microbiology Laboratory in Diagnosis and Control of UTIs
Mira Niazalieva

Therapeutic Challenges of Urosepsis
Hakan Erdem

Prevention of Urinary Tract Infections
Jakhongir Alidjanov

PANEL 6

Improving Quality of Antibiotic Prescribing

Chairpersons:
Mensura Asceric
Salih Hosoglu

Public Campaigns Aimed at Improving the Use of Antibiotics
Stephan Harbarth

The Role of Infectious Diseases Specialist on Antibiotic Consumption
Bojana Beovic

Effect of Governmental Policies on the Antimicrobial Use
Mensura Asceric

Improving Antimicrobial Prescribing Through Knowledge and Skills
Agnes Vechsler Foerdoes

Supported by European Study Group of Antimicrobial Policy (ESGAP)

17:00-18:00

Oral Presentations-II

Chairpersons:
Canan Agalar
Suzana Arapcic

03 June, 2011

Hall A

09:00-09:45

Special Meeting National Infection Control Programs

Chairpersons:
Aida Pilav
Hakan Leblebicioğlu

Hospital Infection Control-Serbian Experience
Biljana Carevic

Infection Control Programs in Turkey
Hakan Leblebicioğlu

Hospital Infection Control-Croatian Experience
Smilja Kalenic

Hall B

09:45-10:15

COFFEE BREAK

Hours

10:15-11:30

PANEL 7

Microorganisms with Oncogenic Potential

Chairpersons:

Peter P. Michielsen
Elmir Cickusic

Mechanisms of Oncogenesis of EBV

Elmir Cickusic

Strategy for Prevention HPV Infection

Nermina Mehinovic

Helicobacter and associated malignancy

Meltem Yalinay Cirak

Viral Hepatitis and Hepatocellular Carcinoma

Peter P. Michielsen

PANEL 8

Management of Chronic Hepatitis

Chairpersons:

Fehmi Tabak
Adriana Vince

The Fight Against Hepatitis: The Turkish Experience

Nefise Oztoprak

HCV Treatment: Where Do We Stand?

Adriana Vince

Treatment of Chronic Hepatitis B

Resat Ozaras

Supported by Turkish Society of Viral Hepatitis (VHSD)

11:30-12:30

SATELLITE-MSD

12:30-13:30

LUNCH

13:30-15:00

PANEL 9

Hepatitis from Bench to Bedside

Chairpersons:

Sukrija Zvizdic
Hurrem Bodur

Microbiological Diagnosis of Viral Hepatitis

Recep Kesli

Imaging in Chronic Hepatitis and in Its Complications

Ismail Mihmanli

Management of Hepatitis C in Drug Users: Experiences from Slovenia

Mojca Maticic

Mini Symposium-Company Arenda

Sead Ahmetagic

PANEL 10

Management of Difficult to Treat Infections

Chairpersons:

Halil Ozsut
Nada Koluder

Management of Diabetic Foot Infections

Halil Ozsut

Management of Invasive Fungal Infections

Omrum Uzun

Treatment of meningitis with MDR Bacteria

Nada Koluder

Supported by Turkish Society of Antimicrobial Agents and Chemotherapy (ANKEM)

15:00-15:30

COFFEE BREAK

15:30-17:00

PANEL 11

Interpretation of Antimicrobial Test Results

Chairpersons:

Turan Aslan
Nezahat Gurler

Current Trends in Beta-Lactamases and Interpretation of Antimicrobial Susceptibility Test Results

Zeynep Gulay

Interpretation and Clinical Aspects of Antimicrobial Susceptibility Test Results: Case Discussions

Guner Soyletir
Cigdem Bal

Supported by Turkish Society of Specialists in Clinical Microbiology (KLIMUD) and Turkish Microbiology Society (TMC)

PANEL 12

Zoonosis: Diagnosis and Epidemiology

Chairpersons:

Mustafa Ertek
Ivo Curic

Molecular Diagnosis of Zoonosis

Riza Durmaz

Clinical and Epidemiological Characteristic of Brucellosis

Sead Ahmetagic

The Treatment Options for Brucellosis

Ivo Curic

Supported by Refik Saydam Health Agency (RSHM)

17:00-18:00

04 June, 2011

Hours	Hall A	Hall B
09:00-09:45	Plenary Lecture III Chairperson: Haluk Vahaboglu The Role of ECDC in the Fight Against Antimicrobial Resistance Dominique Monnet	
09:45-10:15	COFFEE BREAK	
10:15-11:30	PANEL 13 Fungal Infections Among Immune Compromised Patients Chairpersons: Mirela Babic Mine Doluca Candida Infections in Patients with Malignancy Mirela Babic Trends in Antifungal Resistance Among <i>Candida</i> spp. Mine Doluca Aspergillosis in Neutropenia Biserka Troselj	PANEL 14 Antimicrobial Resistance Chairpersons: Fatima Numanovic Teresita Mazzei MDR, XDR, and PDR Superbugs: Global Threats Hsueh Po-Ren PK-PD on Antimicrobial Resistance Teresita Mazzei Laboratory Detection of ESBLs Fatima Numanovic Treatment Approach in MDR Infections Oguz Resat Sipahi <i>Supported by International Society of Chemotherapy (ISC)</i>
11:30-12:30	SATELLITE	
12:30-13:30	LUNCH	
13:30-15:00	PANEL 15 Intestinal Infections Chairpersons: Cafer Eroglu John Wain New Identification Methods for Old Enteropathogens John Wain Travel Associated Diarrhea Salvatore Rubino Clostridium Infection in Hospitalized Patients: Diagnosis and Molecular Epidemiology Burcin Sener Enteric Pathogens in Patients with Diarrhea Selma Pasic	PANEL 16 Acinetobacter Infections-A Multidisciplinary Approach Chairpersons: Maja Ostojic Haluk Vahaboglu Molecular Epidemiology of Acinetobacter Haluk Vahaboglu The Treatment Multidrug Resistant Acinetobacter Infections Emine Alp The Control of Acinetobacter Infections in Hospital Settings Maja Ostojic <i>Supported by Infectious Diseases and Clinical Microbiology Society Specialty of Turkey (EKMUD)</i>
15:00-15:30	COFFEE BREAK	

15:30-17:00

Literature Review in Infectious Diseases in the Last Year

Chairpersons:

Bulent Baysal

Miroslav Petkovic

Vedat Turhan

Ramin Bayramov

Miroslav Petkovic

PANEL 17

Diagnosis and Prevention of Parasitic Infections in Developing Countries

Chairpersons:

Sajma Dautovic-Krkic

Suleyman Yazar

Introduction to Parasitic Infections in Developing Countries

Suleyman Yazar

Diagnosis and Percutaneous Treatment of Hydatid Disease

Necati Ormeci

Echinococcosis in Bosnia

Sajma Dautovic-Krkic

Malaria- Current Views an Ancient Problem

Murat Hokelek

Past and Future: Vaccination Against Protozoan Parasites

Salih Kuk

Discussion

5 June, 2011

Hours

10:00-11:30

Hall A

CLOSING SESSION

Hakan Leblebicioglu

Sead Ahmetagic

Aysegul Karahasan

Nijaz Tihic

Salih Hosoglu

Murat Gunaydin



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Infections in Cancer Patients

Murat Akova

Unit of Infectious Diseases, Department of Internal Medicine, University of Hacettepe, Ankara, Turkey

Several recent reports have indicated that not only a shift in the aetiology of infections and resistance patterns in patients with febrile neutropenia, but also important differences between regions and countries. Viridans streptococcal bacteraemias are common among cancer patients being second only to the coagulase-negative staphylococci. However, in certain centres in Europe gram-negative bacilli have once again become the predominant infecting pathogens. The problems associated with emerging resistance have been widely documented in the literature. In some institutions methicillin-resistance among coagulase-negative staphylococci has reached very high proportions, and in others the incidence of extended-spectrum beta-lactamase producing gram-negative bacilli has risen markedly. These shifts in antimicrobial susceptibility are important in guiding the choice of agents for febrile neutropenia. Antibiotic use and prophylaxis have both been associated with changes in susceptibility, and prescribing habits may influence emerging resistance. In this context, the choice of empirical antibiotic therapy and the use of prophylaxis should be driven by a sound understanding of local circumstances.

Initiating empirical broad-spectrum antibacterial therapy has long been the standard practice for febrile neutropenic cancer patients. Ho-

wever, during the last decade it has become evident that patients with febrile neutropenia do not constitute a homogenous group. The risk factors for developing infection and other major complications vary widely in different subsets of patients with cancer. Therefore, a valuable risk assessment of every febrile neutropenic patient is essential in order to define a tailored therapeutic approach. Those patients with hematological malignancies and severe and prolonged neutropenia will fall into the category of “high-risk”, while others who were treated with less intensive chemotherapies and who were expected to have a short duration (e.g. less than 7-10 days) of neutropenia and fewer complications during the course of neutropenia will be categorized in the “low-risk” group. Recently published “The Multinational Association for Supportive Care in Cancer (MASCC)” risk index has been shown to be a valuable tool for identifying low-risk patients among adult febrile neutropenic cancer patient population. Patients with solid tumors who were treated with conventional chemotherapy and with minimal or no comorbidities (such as mucositis, cellulitis, anorectal infection, pneumonia) will usually be placed into the category of “low-risk”. On the other hand, more intensive chemotherapies have been increasingly used in solid tumor patients and some of them will also undergo an autologous hemato-

poietic stem cell transplantation (AHSCT). This approach will obviously increase the expected duration of neutropenia, the incidence of other comorbidities (e.g. mucositis), and may also affect the hemodynamic and clinical stability of the patient.

Once the patient is stratified in one of the risk groups, several options for empirical treatment exist. Nevertheless, several other factors need to be considered regarding to specific antimicrobial regimen. Among these are local epidemiological pattern of the infecting microorganisms and their antimicrobial resistance pattern. Recent published data indicate that low-risk patients who are able to swallow can successfully be treated with oral antibiotics. The most frequent used regimen for this indication is a combination of a quinolone derivative (e.g. ciprofloxacin) and amoxicillin/clavulanate. Newer quinolones with enhanced activity against gram-positive pathogens (e.g. moxifloxacin, gatifloxacin) have been currently under evaluation for a monotherapy option. This type of therapy is applicable for both inpatient and outpatient settings. Stringent criteria need to be applied for selecting patients who will be treated in an outpatient program which also requires a strong commitment from both patient and healthcare team's side. Another option is to admit the patient to the hospital and treat with parenteral antibiotics until defervescence, and then switch to oral therapy. This provides a viable alternative for patients receiving more intensive chemotherapies for treating cancer with or without AHSCT. Upon switch to an oral regimen the patient could be discharged if his/her clinical condition is permissive. Comparative solid data for such a practice are lacking yet in the literature, however several studies both in IATG/EORTC and in elsewhere are being undertaken on this issue. For the initial parenteral therapy, monotherapy with various beta-lactam antibiotics has been extensively studied comparing with different beta-lactam plus aminoglycoside combinations. The data indicate that monotherapy with a broad-spectrum cephalosporin (e.g. ceftazidime, cefepime) or beta-lactam/beta-lactamase inhibitor combination (e.g. piperacillin/tazobactam) or a carbapenem (i.e. imipenem or meropenem) is as effective as a beta-lactam plus aminoglyco-

side combination for initial empirical regimen. Specific concerns for ceftazidime use exist since this drug has been held responsible for increased incidence of extended-spectrum beta-lactamase producing klebsiella infections in some institutions. Recently published meta-analyses caused concern about cefepime which was found to cause increased mortality in patients due to unexplained reasons. Parenteral quinolones has been less studied for this indication and the data are inconclusive. Therefore quinolones can not be recommended as the initial parenteral agent.

Glycopeptides should not be incorporated into the initial empirical regimen, until a documented gram-positive bacterial infection is observed. Recent data indicate that empirical addition of these agents is also unnecessary in those patients without defervescence after 60-72 hours of empirical broad-spectrum antibacterial therapy. Actually, glycopeptide use should strongly be discouraged unless the patient has a documented gram-positive bacterial infection or has strong predisposing factors to acquire such infections (e.g. clinically documented vascular catheter infection, colonization with methicillin resistant staphylococci or penicillin resistant pneumococci).

In summary, a risk-based approach in patients with febrile neutropenia could be more cost-effective. Various regimens with different antibiotics are available, but specific regimens also need to be tailored to local epidemiological factors.

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Host Immune History and Cross Protection During Pandemic H1N1 Infection

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During the late spring of 2009 pandemic H1N1 emerged in northern Mexico. The pandemic quickly spread and caused serious global health problems and concerns. Interestingly, while pmH1N1 was a novel virus, the overall mortality and morbidity of this virus was similar or less than seasonal H1N1 or H3N2 viruses. We explored human immune responses against pmH1N1 and found several immune profiles that

correlated with disease severity in adults. In animal models we identified specific phases of host immune responses and demonstrated that seasonal influenza viruses could induce cross protection against pmH1N1 through a B cell dependent process. These results suggest that vaccine strategies should take into account that cross protection may be an important consideration in determining the design of influenza vaccines.

Crimean-Congo Hemorrhagic Fever: The Experience in Turkey

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Crimean-Congo hemorrhagic fever (CCHF) is a serious disease caused by the CCHF virus of the Bunyaviridae family. The virus is generally transmitted by a tick bite or through the blood or body fluids of domestic animals or CCHF patients. CCHF was first seen in the Crimean Peninsula in 1940. Today, it has been documented in 30 countries in Africa, Asia, Eastern Europe, and the Middle East. After an incubation period of 1-7 days, the disease is characterized by a sudden onset, with the most common symptoms being high fever, headache, myalgia, fatigue, nausea, vomiting, abdominal pain, and diarrhea.

Epidemiology in Turkey

Despite the incidence of CCHF in Bulgaria, Russia, Iran, and Iraq, countries neighboring Turkey, no case of CCHF was reported from Turkey until 2002. Following a regional epidemic in Turkey in 2003, the disease was determined to be CCHF by laboratory confirmation, and several reports have now been published.

In Turkey, the first cases with findings compatible with CCHF were reported to the Turkish Ministry of Health (MoH) from the city of Tokat in 2002. In 2003, the disease was determined to be CCHF by laboratory confirmation. In 2004, the

total number of cases reached 249, increasing to 266 in 2005, 438 in 2006, 717 in 2007, and 1315 in 2008. The number of cases remained stable in 2009 (at 1318), and then showed a decrease to 868 in 2010. Cases of CCHF and related mortality in Turkey are shown in Figure 1.

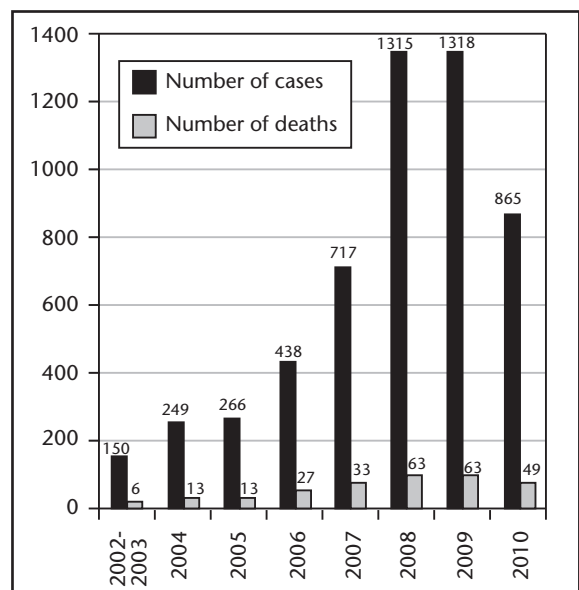


Figure 1. Cases of CCHF and related mortality in Turkey (2002-2010).

hed literature are fatigue, fever, myalgia, headache, loss of appetite, nausea, vomiting, abdominal pain, and diarrhea. In the cases from our country, hemorrhagic findings were detected in almost one-fourth of the cases reported to the MoH between 2002 and 2007.

The rate of cases with hemorrhagic findings has gradually decreased over the years, which may be attributed to diagnosis of cases with mild to moderately severe findings due to the increased awareness of healthcare personnel and patients about the disease. In the cases from our country, thrombocytopenia was the most common laboratory finding (in 93.2% of cases), followed by leukopenia and elevated levels of transaminase.

The mean fatality rate for Turkey is approximately 5%. This rate has not changed over the years and is lower than the rate reported in other series from other parts of the world. The lower fatality rate in Turkey compared to the rates reported by other countries may be due to a better surveillance system, which facilitates the detection of cases with mild to moderate clinical findings, and the relatively better treatment facilities. In the regions where the disease is endemic, diagnosis of cases with mild clinical findings due to the education and increased awareness of the healthcare personnel and public may have contributed to the low fatality rate. In addition, the CCHF strain determined in our country is significantly homologous with the strain detected in Russia and Kosovo (former Yugoslavia). In CCHF cases caused by similar strains, the fatality rate has been found to be lower than those of other regions.

Thrombocytopenia of $\leq 20 \times 10^9/L$, a prolonged activated partial thromboplastin time (aPTT) ≥ 60 s, melena, somnolence, diarrhea, hematemesis, hematuria, elevated alanine aminotransferase (ALT) and lactate dehydrogenase (LDH), and viral load $\geq 1 \times 10^9$ RNA copies/mL were reported as independently associated with mortality.

Diagnosis

In 2003, before the diagnosis of the disease was established, a Scientific Commission set up by the Turkish MoH described the cases and developed a case report form. The MoH instructed that the approach to such cases be in compliance with these case descriptions. In the same year, serum samples were found positive for the disease

by the National Reference Center for Arbovirus and Viral Hemorrhagic Fevers, Pasteur Institute, Lyon, France. After 2004, serum samples were studied by the virology laboratory of Refik Saydam Hygiene Center. Patient serum samples were tested for anti-CCHF IgM and IgG antibodies by ELISA. CCHF virus RNA was investigated by RT-PCR, and direct sequence analysis was performed in this center.

Treatment

Supportive therapy including replacement of blood and clotting factors is crucial in severe patients. Currently no antiviral agent for the treatment of CCHF has been approved by the Food and Drug Administration or European Medical Agency. Ribavirin has been shown to be effective against several hemorrhagic fever viruses such as Rift Valley fever virus, Hantaan virus and Lassa virus. It has been shown to inhibit *in vitro* viral replication of the CCHF virus. Oral ribavirin has been recommended by the World Health Organization (WHO) as a potential therapeutic agent for CCHF; however, the treatment efficacy of ribavirin remains unclear. A review of the literature reveals studies reporting the efficacy of ribavirin in the treatment and prophylaxis of CCHF; but there are also published studies reporting that ribavirin has no effects on mortality or viral load. Most of the CCHF patients in Turkey in 2004 received ribavirin. Ribavirin usage decreased gradually thereafter because of the findings suggesting its ineffectiveness on mortality and viral load. Though a few studies reported recently that ribavirin is effective in the early phase of CCHF, a quasi-experimental study reported that oral ribavirin usage can even be harmful in the first eight days of the disease. An intravenous formulation of ribavirin was administered in a limited number of patients and was also determined to have no effect on mortality. A recent randomized study investigating the efficacy of ribavirin found no positive effect on mortality and the other evaluated laboratory parameters. Since there has been no randomized placebo-controlled double-blind study, the effect of ribavirin in CCHF remains to be clarified.

Prevention and Control

The MoH has described the centers that can treat patients according to the disease severity,

case definitions and referral criteria. Treatment options, isolation measures, suggestions for disinfection, and the approach in handling the decreased were published in a small pamphlet and sent to all health centers. Epidemiological data have been collected since 2004 using the standard case reporting forms developed by the CCHF Scientific Committee.

Brochures and posters were prepared to educate the public and healthcare workers. Healthcare workers in the most prevalent cities were educated in particular. A collaboration was established with the Ministry of Agriculture and Rural Affairs regarding tick combat in livestock. The algorithms regarding case management of tick contact were prepared and distributed to all healthcare centers. A guide was prepared for standard control measures and protection of healthcare personnel. Face-to-face education was conducted in the endemic area in 2009 and 2010. The referral center was reorganized in 2010 to decrease the intensive work load in certain centers.

The epidemic seems to be self-limiting in Turkey. Experience gained from this situation will be useful in managing CCHF outbreaks in other countries.

Acknowledgement

Thanks the members of CCHF Scientific Committee, coordinated by Ministry of Health in Turkey.

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Tularemia: Laboratory Diagnosis and Molecular Epidemiology

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Francisella tularensis, the causative agent of tularemia, has been recognized as a zoonotic and human pathogen for a century. The genus *Francisella* is currently divided into five species, mainly on the basis of 16S rDNA sequencing and fatty acid composition: *F. tularensis*, *F. philomiragia*, *F. piscicida*, *F. noatunensis*, and *F. hispaniensis*. According to the geographical distribution, epizootiology, biochemical characteristics, and virulence assay in rabbits, four subspecies (subsp.) of *F. tularensis* have been distinguished to date: *F. tularensis* subsp. *tularensis*, subsp. *holarctica*, subsp. *mediasiatica* and subsp. *novicida*. Although all have been associated with human disease, subsp. *tularensis* and *holarctica* are of particular clinical and epidemiological relevance.

Laboratory Diagnosis of Tularemia

Laboratory diagnosis of tularemia can be examined in two parts: specific (microbiological) and non-specific routine-laboratory investigations. Non-specific routine laboratory investigations, serum chemistry and routine peripheral blood count, do not provide diagnostic clues for tularemia apart from non-specific inflammatory signs such as leucocytosis, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) elevation.

Microbiological Diagnosis

Microbiological diagnosis can be classically divided into “Direct and indirect” methods. Direct diagnostic methods include (i) microscopic demonstration of *F. tularensis* (apart from histopathological examination), (ii) culture, (iii) molecular methods and (iiii) Antigen detection by ELISA or immunochromatographic assay (ICT). Indirect diagnostic approach relies on the serology that is the most common used method for the diagnosis of tularemia.

Direct Diagnostic Methods

Direct examination should be applied for clinical specimens and confirmation of suspected cultures. *F. tularensis* may be identified by direct examination of fresh clinical specimens (ulcer and wound swab, secretions, exudates, or biopsy specimens) using Gram stain, direct fluorescent antibody (DFA) or immunohistochemical stains (IHC). Under microscopic examination of Gram-stained specimens and cultures, *Francisella* appear so tiny, pleomorphic, and poorly staining gram-negative coccobacillus (0.2 to 0.5 by 0.7 to 1.0 μm) mostly as single cells. The Gram stain interpretation may be difficult because the

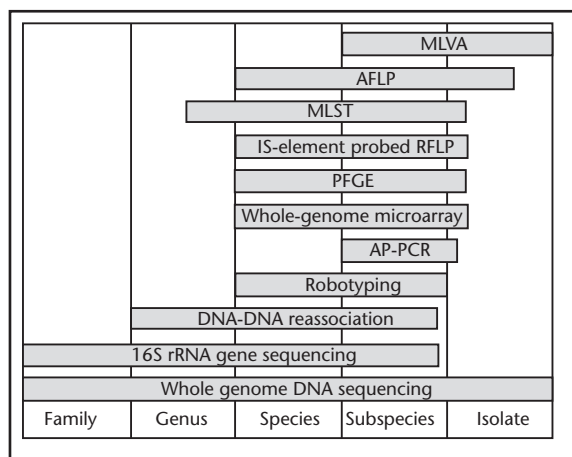


Figure 1. Resolution of typing methods. This scheme depicts the approximate taxonomic ranges of discrimination of various genetic typing methods applied to *Francisella*²⁶.

cells are minute and faintly staining, so can be easily missed. Direct Gram staining, therefore, is of no diagnostic value.

To improve visualization, DFA staining using a labeled hyperimmune polyclonal antibody presumptively identified subsp. *tularensis* and subsp. *holarctica* was developed. Microscopic demonstration of *F. tularensis* using fluorescent-labeled antibodies is a rapid diagnostic procedure; test results can be available within several hours of receiving the specimens. IHC, immunoelectron microscopy and immunofluorescence employing specific antibodies are also valuable tools to detect the pathogen in sputum, pus, as well as in formalin-fixed, paraffin-embedded tissues.

The presence of *F. tularensis* in specimens taken from environment (animal feces, urine, water, hay, mud, and ectoparasites) and patients (ulcer, wound, tissues) may be determined by ELISA and lateral flow assay.

Culture

Unequivocal diagnosis of tularemia requires isolation of the causal agent (gold Standard). The primary diagnostic challenge with tularemia infections, particularly with *F. tularensis* subsps. *tularensis* and *F. tularensis* subsps. *holarctica*, is the difficulty encountered when trying to culture the organism from a clinical sample.

F. tularensis, are slow-growing, fastidious organisms requiring sulfhydryl compounds (cysteine, cystine, thiosulfate, and isoVitaleX) and 24-

72 h for growth on artificial media. However, some strains of *F. tularensis* lack an overt requirement for cysteine or enriched medium for growth. Cysteine enriched media enhance the growth of *F. tularensis*, but are not required for growth of isolates of *F. tularensis* subsp. *novicida* and *F. philomiragia*. *F. tularensis* do not grow on most routine solid media or on gram-negative selective media such as MacConkey or eosin methylene blue agars (EMB).

Specimens should be taken on the basis of clinical presentation and before administration of antibiotics. Various cysteine-supplemented agars are acceptable for growing *F. tularensis*, which include glucose cysteine blood agar (GCBA), cysteine heart agar with 9% chocolatinized sheep blood (CHAB) agar, Chocolate agar (CA), modified Thayer-Martin (TM) agar, buffered charcoal yeast extract (BCYE). *F. tularensis* grows slowly (generation time: 60 min), even on appropriate media; therefore, 2-4 days are often required for robust growth to be observed on agar plates. Blood agar may support growth of some *F. tularensis* isolates on initial plating but not upon subsequent passage. Although it grows poorly or not at all on most ordinary media, it is occasionally isolated using automated blood culture systems. Culture should be incubated at 35-37°C de aerobically and observed daily for 10-14 days. On the other hand, though *Francisellae* are strict aerobes, *F. tularensis* grow better with increased CO₂ (5-10%).

While *F. tularensis* grows poorly at 28°C, *F. tularensis* subsp. *novicida* and *F. philomiragia* grow well. Growth on MacConkey agar or in nutrient broth containing 6% NaCl will differentiate *F. tularensis* subsp. *novicida* and *F. philomiragia* from subsp. *tularensis* and *holarctica*.

F. tularensis is rarely isolated from blood cultures, with existing literature consisting primarily of case reports. The recovery of *F. tularensis* from contaminated specimens or environmental samples may be facilitated by the addition of antibiotics to the media. Suspected colonies are confirmed by slide agglutination with *F. tularensis* antiserum, DFA, PCR or cellular fatty acid composition analysis. *F. tularensis* is also notorious for causing laboratory acquired infections. Biosafety Level 2 (BSL-2) is sufficient for laboratory handling of routine clinical specimens, but

all procedures in processing isolates suspected of being *F. tularensis* should be performed in Biological Safety Level-3 (BSL-3) practices.

Serologic Testing

Serology has been the most commonly used laboratory approach for the diagnosis of tularemia over the past 80 years. However, specific antibody responses are typically not detectable prior to two weeks of the disease with currently available tests and cross-reactivity with other organisms remains an issue.

IgM, IgA and IgG antibodies appear simultaneously after initial infection and IgM antibodies can last for many years. Antibodies to *F. tularensis* may be detected as early as first week after onset of symptoms. Antibodies may be demonstrated by tube agglutination, microagglutination, hemagglutination, and enzyme-linked immunosorbent assay.

The MAT remains the most common method used to detect antibodies against *F. tularensis* and is considered as the current reference method for the serodiagnosis of tularemia. In the presence of compatible symptoms, sustained high TA titer of $\geq 1:160$ or MAT titer of $\geq 1:128$ in an acute specimen support a presumptive diagnosis of tularemia. Antibodies may cross-react with *Brucella* spp., *Proteus* OX19, and *Yersinia* spp., but titers to *F. tularensis* are almost always higher. False-positive heterophile agglutinins also rarely occur during tularemia.

Enzyme-Linked Immunoassay (ELISA): ELISA enables qualitative and quantitative measurement of different antibody classes, i.e. IgM, IgG and IgA in serum or plasma. In contrast to several other infections, the role of different immunoglobulin subclasses in the diagnosis of acute tularaemia is not yet determined due to the extreme long persistence of *Francisella*-specific antibodies after infection. Although ELISAs, is purported to be more sensitive and specific than agglutination for the diagnosis of tularemia, their limitation of host specificity preclude their wide use in serosurveillance. ELISA result should be confirmed by a different second method which normally is an immunoblot. Today, two-step approach for the serological diagnosis of tularaemia with a combination of a screening test (ELISA) and a conformational test (immunoblot) might prove to be a feasible.

Western blot (WB): WB provides the detection of IgG antibodies directed to the lipopolysaccharide of *F. tularensis* in human serum samples. Western blot analysis can detect the antibody responses to 17- and 43-kDa *F. tularensis* proteins in the serum.

Detection of Cell-Mediated Immunity in Tularaemia

A delayed-type hypersensitive reaction detected by the skin test was previously used to measure specific reactivity by means of an intradermally injected ether extract of *F. tularensis*. This test is no longer used due to lack of standardization. The demonstration of a *F. tularensis*-specific T-cell response such as whole blood IFN- γ release assay *in vitro* has been proved to be a potential diagnostic means. *F. tularensis*-specific T-cell response may be positive earlier than serologies. However, this method is time-consuming and restricted to specialized laboratory because of the lack of standardized antigen preparations and commercially unavailable.

Other Techniques

ICT represents alternative techniques for the rapid diagnosis of *F. tularensis*. ICT, developed by Spletstoeser et al. from Bundesweir, Germany, efficiently detects *F. tularensis*-specific antibodies in sera from humans and other mammalian species (nonhuman primate, pig, and rabbit). This rapid test preferentially detects IgG antibodies that may occur early in the course of human tularemia. Another commercially available ICT, **VI-Rapid® TULAREMIA (Vircell, SL Granada, Spain)** enables the qualitative detection of total antibodies (IgG + IgM + IgA) against *F. tularensis* in both serum and plasma samples. This kit displayed excellent performance (99.1% sensitivity and 98.6% specificity) and rapid detection-visual reading in just 15 minutes.

Molecular Methods for Detection, Identification and Typing of *F. tularensis*

A wide variety of PCR assays have been developed for the detection of *F. tularensis* DNA in both clinical and environmental specimens (Table 1). PCR is a useful diagnostic tool for the diagnosis of tularemia. The majority of PCR tests for *F. tularensis* have been gel-based PCR assays targeted at the genes encoding the outer memb-

Table 1. PCR platforms for *Francisella tularensis*⁸

Christensen et al.	fopA tul4	50 fg/27 genomic equivalents for both assays	Comparison of three different, real-time PCR platforms
Fulop et al.	fopA	1 CFU direct detection, 10 ² CFU/mL in blood	None
Fujita et al.	fopA	Ten DNA copies	None
Grunow et al.	tul4	10 ² CFU/mL in saline, 10 ³ -10 ⁴ in spiked serum	Detected <i>F. tularensis</i> from tissue samples from infected European brown hares
Higgins et al.	TaqMan 5' nuclease assay: <i>fopA</i> PCR-EIA: <i>tul4</i>	< 100 CFU for both assays	Successful detection of <i>F. tularensis</i> in mouse tissue and ticks
Junhui et al.	Three primers		PCR (38 out of 46) better than cultures (22 out of 46) for blood samples from infected mice
Skottman et al.	23kDa	1 fg sensitivity	Part of multiplex PCR for biodefense detection. Tested in infected hares
Tomioka et al.	tul4	50 CFU/mL in spiked human blood samples	Part of multiplex PCR array for biodefense detection. Used LVS <i>F. tularensis</i> for testing
Versage et al.	<i>isftu2</i> element and the 23kDa and <i>tul4</i>	<i>tul4</i> : 1 CFU <i>isftu2</i> element and 23kDa: <1 CFU	More sensitive than culture during assessment of environmentally contaminated samples

rane proteins, fopA or tul4. These PCR assays show good specificity and allow for rapid detection of *F. tularensis* in specimens.

Refinements to PCR techniques have focused on improving the limits of detection and processing time and developing the testing for field use. In order to improve detection of *F. tularensis* from complex specimens, such as environmental samples, Versage et al. developed a multitarget PCR, with assays for the *isftu2* element and the 23kDa and *tul4* genes, and this platform proved to be more sensitive than culture when comparing samples from infected animal carcasses.

Molecular subtyping: PCR subtyping assays have been developed for discriminating *F. tularensis* subsp., in the absence of a culture. Recently, a gel-based PCR assay targeted at the region of difference 1 (RD1), has been reported to distinguish between all four subspecies of *F. tularensis*.

Molecular Typing Methods

Rapid and accurate typing procedures are crucial for epidemiologic surveillance, and investigation of outbreaks. In addition to PCR assays, which allow the rapid detection of all *F. tularensis* strains, several molecular methods such as repetitive extragenic palindromic element PCR (REP-PCR), enterobacterial repetitive intergenic consensus sequence PCR (ERIC-PCR), random amplified polymorphic DNA PCR (RAPD-PCR), long primers (LP)-RAPD-PCR, to discriminate between subspecies or even strains were developed. Recently, a family of tandem repeats located within a repeated sequence and present in multiple loci in the *Francisella* genome was applied for fingerprinting of *F. tularensis*. Resolution of different typing methods is given in Figure 1.

PFGE, AFLP, regional difference (RD) analysis, and MLVA represent methods for sampling genomic sequence diversity. These four methods

have been used to successfully assign *Francisella* isolates to subspecies and to identify major population clades within the subspecies. Resolution below the subspecies level is dependent upon how extensively these approaches are applied, as additional levels of restriction digestion or primers can be employed to increase resolution.

MLVA that capitalizes upon hypermutable tandem repeats and locus-specific PCR amplification is a high resolution method. The analysis of short-sequence tandem repeats, or variable number tandem repeats, has been capable of identifying both subspecies and subdivisions within the subspecies, probably due to inclusion of both low- and high-diversity loci. In addition, its high resolution makes MLVA very useful for epidemiological and forensic analysis of outbreaks. MLVA will continue to be an important subtyping tool, although this will be more and more in the context of distinguishing among isolates within major groups that are first defined by MLST, SNP, RD, or whole genome analysis.

Unlike *F. tularensis* subsp. *holarctica*, *F. tularensis* subsp. *tularensis* is further subdivided into two genetically distinct populations (A.I and A.II) that differ with respect to geographical location, anatomical source of recovered isolates, and disease outcome. The geographic distributions of the A.I. and A.II. subpopulations are associated with distinct abiotic and biotic factors, including known tularemia vectors and hosts. The spatial distributions of these 2 subpopulations are associated with large differences in elevation, with A.I. occurring at lower elevations than A.II. MLVA provided complete discrimination among *F. tularensis* subsp. *tularensis* A.I. isolates, with the exception of 3 sets of isolates obtained from the same hosts. Among A.II. isolates, all but 2 sets of isolates were resolved by MLVA.

A study by Vogler et al., based on the result of whole-genome single nucleotide polymorphism (SNP) analysis, high-density microarray SNP genotyping, and real-time-PCR-based canonical SNP (canSNP) assays, 11 subclades within *F. tularensis* subsp. *holarctica* were observed. These subclades include a new, genetically distinct subclade that appears intermediate between

Japanese *F. tularensis* subsp. *holarctica* isolates and the common *F. tularensis* subsp. *holarctica* isolates associated with the radiation event (the B radiation) wherein this subspecies spread throughout the northern hemisphere. Their phylogenetic analyses suggest a North American origin for this B-radiation clade and multiple dispersal events between North America and Eurasia.

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Vector Borne Diseases-an Update

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Vectors are the transmitters of diseases causing organisms that carry the pathogens from one host to another. By common usage vectors are usually arthropods because they account for over 85% of all known animal species, and they are the most important disease vectors.

Vector-borne diseases are infections transmitted by the bite of infected arthropod species, such as mosquitoes, ticks, triatomine bugs, sandflies, and blackflies.

The most significant mode of disease transmission by vectors is by biological transmission by blood-feeding arthropods. Mechanical transmission of disease agent may also occur.

Occuring of these diseases is caused by the existence of sources of infection, the vector-carrier and suitable hosts, which is associated with environmental factors, as well as with different demographic and social factors.

Vector-borne diseases are widespread around the world, but the highest number of cases occur

in tropical and subtropical areas because there are favorable conditions of living for a large number of vectors. In the 17th and 18th century in these areas, vector borne diseases represented a major public health problem. The implementation of control and preventive measures reduced the number of patients, and some diseases are completely eradicated.

After this period, necessary attention was not paid to these diseases, implementation of preventive measures stopped and many socio-demographic and environmental factors were favorable for increasing the number of vectors. Climate changes are changing the morbidity and mortality of infectious disease. Because of that at the end of the 20th century was a trend of re-growth of these diseases, which is still ongoing.

In this paper will be given one up-date and current status of vector-borne diseases around the world or and the most important risk factors for them.



Hospital Infection Control in Bosnia and Herzegovina

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Prevention and control of nosocomial infections is the responsibility of all individuals and services providing health care. The major preventive effort should be focused in hospitals and other health care facilities. The responsible health authority should develop a national (or regional) programme to support hospitals in reducing the risk of nosocomial infections and designate an agency to oversee the programme (a ministerial department, institution or other body), and plan national activities with the help of a national expert committee. Professional and academic organizations must also be involved in this programme.

In former Yugoslav countries, there was no effective infection control and similar situation was in other former socialist Balkan countries. Therefore, since 2003 IFIC (International Federation of Infection Control) have established a regional network among hospital infection control professionals in countries in Southeast Europe (Albania, Bulgaria, Croatia, Greece, Hungary, UNMI Kosovo, Former Yugoslav Republic of Macedonia, Romania, and Slovenia). Bosnia and Herzegovina has also become part of this network. Main goals were to establish a functioning network to support infection control education

and communication in these countries, and to determine whether networking between countries will increase the number of hospital infection control programs in the whole region. Implementation of measures to prevent and control nosocomial infection in our country takes place through the Infection Control Team, Commissions for Control of Hospital Infection, Epidemiological Service of the Institute of Public Health and Ministry of Health.

Commissions for Control of Hospital Infection provides a forum for multidisciplinary input and cooperation, and information sharing. This Commission include wide representation from relevant programmes: e.g. management, physicians, other health care workers, clinical microbiology, pharmacy, central supply, maintenance, training services. The commission have a reporting relationship directly to either administration or the medical staff to promote programme visibility and effectiveness. In an emergency (such as an outbreak), this committee is able to meet promptly. The Infection Control Team is responsible for the day-to-day functions of infection control, as well as preparing the yearly work plan for review by the Commissions for Control of Hospital Infection and administration.

Since 2004 the Clinical Center of the University in Sarajevo, established a laboratory for hospital infection control which exceeds in the department in 2008. A manual for prevention of nosocomial infection compiling recommended instructions and practices for patient care, as important tool are designed and implemented in all hospital departments. The manual is developed and updated by the laboratory, with review and approval by the Commission for Control of Hospital Infection. The department is responsible for: screening of patients and staff as needed, handling patient and staff specimens to maximize the likelihood of a microbiological diagnosis, developing guidelines for appropriate collection, transport, and handling of specimens, ensuring laboratory practices meet appropriate standards, ensuring safe laboratory practice to prevent infecti-

ons in staff, performing antimicrobial susceptibility testing following internationally recognized methods, monitoring mechanisms of resistance and providing summary reports of prevalence of resistance, monitoring sterilization, disinfection and the environment where necessary, timely communication of results to the Commission for Control of Hospital Infection, epidemiological typing of hospital microorganisms. This way of the organization has proven to be successful in the prevention and control of nosocomial infections in our hospital. Future plans in the field of control of nosocomial infections in our country should include the education improvement and development of a surveillance program on the state level as essential first step to identify problems and priorities, and evaluate the effectiveness of infection control activity.

Intensive Care Unit Acquired Bloodstream Infections-Impact of the Patient's Age

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Introduction: Nosocomial infections are the rising problem of modern medicine. Among them, the intensive care unit (ICU) acquired infections are the major issue of concern because of their high incidence and excessive negative impact on morbidity, mortality and overall hospital costs. In correlation to progressive aging of population, the rate of patients ≥ 65 years treated in ICU is on the increase. Little is known about the relationship between older age and ICU-acquired infections.

Objective: To assess the relationship between older age and risk for acquisition of ICU acquired bloodstream infections (BSI), determine their epidemiology and the impact of the patient's age on the clinical outcome.

Design: Retrospective analysis of prospectively collected cohort of ICU patients.

Setting: ICU of the University Hospital for Infectious Diseases, Zagreb.

Patients: Mechanically ventilated (MV) infectious disease patients of both sexes ≥ 18 years, treated in ICU ≥ 48 hours from 1994-2008.

Methods: Standard tests for uni- and bivariate analyses, multivariate analysis (logistic regression), „propensity score“ calculation.

Outcome variables: Primary: acquisition of BSI; secondary: duration of ICU stay, overall and 28-day survival rate in ICU.

Results: Of 1093 included patients 46.6% were ≥ 65 years. The elderly patients had higher rate of BSI (26.1 vs. 21.1%, $p=0.484$) and higher mortality rate (52.7 vs. 42.8, $p=0.0010$). Among patients with BSI 52% were ≥ 65 years, 53.1% were female, and 59.5% had CNS infection. The patients with BSI had lower age-adjusted APACHE II score (mean 15.3 vs. 17.7, $p\leq 0.0001$) and higher GCS (mean 11.2 vs. 10.2, $p=0.0005$), longer insertion of CVC (mean: 25.6 vs. 10.9 days, $p\leq 0.0001$), longer duration of MV (mean: 28.3 vs. 10.1 days, $p\leq 0.0001$), but they had higher survival rate (59.8% vs. 50.3%, $p=0.0079$). Multivariate analysis showed no correlation between age and BSI acquisition (OR= 0.992, 95% CI: 0.712-1.381). Because of imbalance between groups, the propensity scores for acquiring BSI were calculated and further analysis of clinical outcomes was performed on 212 adjusted pairs of the patients. Although showing significantly longer ICU stay, clinical outcome analyses suggest a tendency of higher survival rate among patients ≥ 65 years with BSI ($p=0.0686$) and sho-

wed higher 28-days survival among them ($p=0.047$). The etiology of BSI was similar in both observed age-groups ($p=0.4940$); out of a total of 353 episodes of BSI in 256 patients, 32.0% were caused by non-fermenting gram-negative bacteria, 24.1% by enterobacteria, 18.1% by gram-positive bacteria, 17.6% were polymicrobial, 7.1% caused by *Candida* and 1.1% by other bacteria. Of 353 episodes of BSI, 14.2% were caused by ESBL and third-generation cephalosporin-resistant bacteria, 9.3% by MRSA, 1.1% by ampicillin-resistant enterococci, 4.5% by multidrug-resistant and 3.4% by carbapenem-resistant non-fermenting gram-negative bacteria.

Conclusion: Elderly patients represented a high proportion among observed patients. Although the proportion of patients with BSI and the overall mortality rate was higher among patients ≥ 65 years, multivariate analysis showed no correlation between age and BSI acquisition. Clinical outcome analysis showed a significantly longer ICU stay, but better overall and 28-day survival rate among patients ≥ 65 years with BSI. No differences were found in etiology and resistance pattern of BSI episodes between the observed age-groups.



Setting Up Sterilization Units in Health Care Settings

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Being aware of the fact that problems can and do occur is probably the most important step towards solving them.

This undoubtedly applies to “sterilization” as well. One of the bottlenecks is that the differences in quality between Central Sterile Supply Departments (CSSD) is still too big. Some departments approach the “state of the art” level, others, in contrast, keep on providing medical devices of an unacceptable quality. This is our “inconvenient truth”, which we should urgently deal with. That is only possible through sharing knowledge and through cooperating; in other words a “collective” approach within the framework of a national society is the fastest way to “individual” progress.

Good sterilization practices are built on three foundations: people, means and knowledge. Each of them is necessary in order to arrive at a good result. In this presentation I discuss mainly the means that are necessary to set up a good department. Different “technical aspects” of sterilization are illustrated by means of a practical example: the setting up of a new department in the General Hospital St Jan (Bruges, Belgium).

First the development of the CSSD in this hospital is put into an historical perspective.

Then the recent renovation of the CSSD is discussed. The history of the hospital, namely, goes back to the Middle Ages. It is noteworthy that only in the 19th century it was decided that a more modern hospital building had to be constructed. There, 50 years ago, a more or less centralized CSSD treated mainly compresses, linen drapes, glass syringes etc.. Later on, also surgical instruments were packaged and sterilized. From the opening, in 1977, of a new hospital, outside the city, all instruments were cleaned and sterilized in the CSSD. But after 15 years the department didn't meet the “state of art” anymore. Only after insisting for a long time a new location within the hospital was assigned to the CSSD.

An architect drew the basic plan in consultation with senior staff of the department. Hereby a number of essential requirements were taken into account: the available surface area, the flows of goods which may not cross, the separation of the different zones, sluices that have to separate unclean, clean and sterile areas from the “outside world” etc.

An answer to the crucial question how big, theoretically, a department should be, is sought and found in the brochure “Architecture et locaux en stérilisation” of the Association Française

de stérilisation (AFS). Because of efficiency and ergonomics there is a trend today to limit the surface of the unit.

Furthermore various technical aspects such as air treatment, the finishing of the floors, walls and ceilings are discussed. Happily, in order to address them in the AZ St Jan, a team of experts was appointed. It is very important that also the CSSD participates in the meetings of that team to avoid costly mistakes and compromises on architectural and functional principles.

The different spaces are discussed in detail and the capacity and number of washer-disinfectors and steam sterilizers, are calculated. Hereby, certainly, an increase of activities in the future should be taken into account.

Only a multidisciplinary approach can guarantee an end result that is bigger or better than the simple addition of the separate elements.



International Standards on Sterilization of Medical Devices

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Standard is the state of being the same in production, mentality and measurement. Standardization is creating rules for an application and to put the rules into practice. Standardization is important for production to find out quality levels of product. Moreover, the main purpose of standardization of sterilization is patient safety. Harmonized standards are prepared and approved by European Committee members and are mandatory regulations in production and application.

Medical Device Directives

There are three important directives about medical devices approved by European Committee member countries:

1. Medical Devices Directive - 93/42/EEC
2. Active Implemantable Medical Device Directive-90/385/EEC
3. In Vitro Diagnostic Devices Directive-98/79/EEC

According to these directives, member states have to take all necessary steps to ensure that devices may be placed on the market and put into service only if they do not compromise the safety and health of patients, users and, where appli-

cable, other persons when properly installed, maintained and used in accordance with their intended purpose.

The definition of “sterilization” is complete elimination or destruction of all forms of microbial life including endospores. According to EN 556-1; 2001: Sterilization of medical devices-Requirements for medical devices to be designated “STERILE”, Part 1: Requirements for terminally sterilized medical devices; for a terminally-sterilized medical device to be labeled “STERILE”, the theoretical probability of there being a viable microorganism present on the device shall be equal to or less than one in 1×10^{-6} . Only in this way, it is possible to talk about “sterility assurance level (SAL)” which is also the assurance for patient safety.

Standards About Packaging

ISO 11607 “Packaging to sterilize medical devices”

Part 1: Requirements for materials, sterile barrier systems and packaging

Part 2: Validation requirements for forming, sealing and assembly processes

EN 868 “Packaging for terminally sterilized medical devices”

Part 2: Sterilization wrap

Part 3: Paper for use in the manufacture of paper bags (specified in EN 868-4) and in the manufacture of pouches and reels (specified in EN 868-5)

Part 6: Paper for low temperature sterilization processes

Part 8: Re-usable sterilization containers for steam sterilizers conforming to EN 285

Part 9: Uncoated nonwoven materials of polyolefines

Standards for Sterilizers

EN 285 “Steam sterilizer”: This is the most important standard in producing steam sterilizers to use healthcare settings. In all member countries should have steam sterilizers in their healthcare settings compatible with this standard.

EN 1422 is about technical details of Ethylene Oxide sterilizers and **EN 14180** is about low temperature steam formaldehyde.

Standards About Monitoring Sterilization Process

Monitorization of sterilization process is a major concern all over the world. Although there are different methods for monitoring, all of them must be compatible with international standards to ensure patient safety. These are the most important standards about monitoring different sterilization methods:

ISO 11137 “Sterilization of health care products - Radiation -Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices”

ISO 17665 “Sterilization of health care products-Moist heat- Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices”

ISO 10993 “Biological evaluation of medical devices -Part 7: Ethylene oxide sterilization residuals”

ISO 11135 “Sterilization of health care products-Ethylene oxide-Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices”

ISO 14937 “Sterilization of health care products-General requirements for characterization

of a sterilizing agent and the development, validation and routine control of sterilization process for medical devices”

ISO 17665-Sterilization of health care products - Moist heat- Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices

Standards and Classification of Indicators

Monitoring of sterilization process is performed by using physical, chemical and biological indicators. These standards guide us how to choose indicators and how to evaluate the results.

ISO 14161 “Sterilization of health care products-Biological indicators-Guidance for the selection, use and interpretation of results”

ISO 15882 “Sterilization of health care products-Chemical indicators-Guidance for selection, use and interpretation of results”

ISO 11140 “Sterilization of health care products-Chemical indicators-Part 1: General requirements”.

In this standard chemical indicators are classified as below:

Class 1: Process indicators are intended for use with individual units (e.g. packs, containers) to indicate that the unit has been directly exposed to the sterilization process and to distinguish between processed and unprocessed units. They are designed to react to one or more of the critical process variables.

Class 2: Indicators for use in specific tests like Bowie-Dick test. They are intended for use in specific test procedures as defined in relevant sterilizer/sterilization standards.

Class 3: Single variable indicators are designed to react to one of the critical variables and are intended to indicate exposure to a sterilization process at a stated value (SV) of the chosen variable.

Class 4: Multi-variable indicators are designed to react to two or more of the critical variables and are intended to indicate exposure to a sterilization cycle at SVs of the chosen variables

Class 5: Integrating indicators are designed to react to all critical variables. The SVs are generated to be equivalent to, or exceed the performance requirements given in the ISO 11138 series for BIs.

Class 6: Emulating indicators are cycle verification indicators which are designed to react to all critical variables for specified sterilization cycles. The SVs are generated from the critical variables of the specified sterilization process.

ISO 11138-“Sterilization of health care products-Biological indicators”

To be able to choose the best indicator for our hospitals is really a big deal. Although there are so many performance tests written in ISO 15882 and 14161 to evaluate the indicators, it is not possible to perform these tests on our own. These tests have to be done using special equipment like resistometer. Equipment for testing is described in **ISO 18472**-“Sterilization of health care products-Biological and chemical indicators-Test equipment”.

Standards Related to Quality Control

ISO 13485-“Quality control standard for medical devices”: According to this standard, medical device producers and the users have to set up quality control system in their settings, have process documentation, and obey strictly to the rules of quality control.

ANSI/AAMI ST79: 2006 is another important standard valid in United States. According to this standard all the steps given below have to be documented:

1. Cleaning:

- a. Water and detergent quality
- b. Print-outs of washer disinfectors including physical parameters
- c. Chemical control results
 - Protein or ninhydrin-equivalent test results
 - Test Object for Surgical Instruments (TOSI) results

2. Traceability:

- a. Tray badges including the ingredients, cycle number, cycle date, expiry date, name of the staff doing the cycle and etc.

3. Sterilization efficacy:

- a. Cycle monitorization results
- b. Physical and if necessary chemical and biological indicator results
- c. Bowie-Dick and vacuum-leak test results
- d. Qualification test results of sterilizers
- e. Calibration and validation reports

4. Recalling reports:

- a. Reason for recall
- b. Recalled items and departments
- c. Recalled but used instruments
- d. Official information for infection control team
- e. Resterilization reports of recalled instruments
- f. Corrective action reports

5. Routine maintenance reports:

- a. Date
- b. Reason
- c. Maintenance report
- d. State of machine after maintenance

In conclusion, international standards are very important guidelines for sterilization of medical devices in healthcare settings. Using these standards is the first positive step in order to ensure patient safety and quality in hospitals.

Disinfection of Endoscopes

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Flexible endoscopes are complex reusable instruments that require unique consideration with respect to decontamination. Although endoscopic equipment has been implicated in transmitting infection, all transmissions have been due to errors in the process of cleaning and disinfecting the equipment or in breakdown of general infection control practices. Other potential risk factors for transmission of infection at endoscopy include the use of older endoscopes with associated surface and working channel irregularities, and the use of contaminated water bottles or irrigating solutions.

In addition to the external surface of endoscopes, their internal channels for air, water, aspiration and accessories are exposed to body fluids and other contaminants. In contrast to rigid endoscopes and most reusable accessories, flexible endoscopes are heat labile and cannot be autoclaved.

In 1968 Spaulding proposed classifying medical devices into three groups according to the risk of infection related to their use:

- Critical devices are those that enter sterile tissue or vascular spaces (eg, biopsy forceps, papillotomy devices). These devices should be sterilized.
- Semi-critical devices are those that contact the mucous membranes (eg, upper and lower

gastrointestinal endoscopes). These devices require high-level disinfection designed to destroy all microorganisms except some bacterial spores.

- Non-critical devices only contact skin (e.g., blood pressure cuffs) and need not be sterilized or subjected to disinfection procedures.

Gastrointestinal endoscopes meet the definition of semicritical devices. Thus, most organizations recommend high-level disinfection (HLD) as appropriate for these instruments.

Steps of Endoscope Disinfection

Endoscope reprocessing can be divided into six separate stages: pre-cleaning, leak testing, cleaning, high-level disinfection, rinsing, and drying.

Pre-cleaning: Decontamination should begin as soon as the endoscope has been removed from the patient. Before the endoscope is detached from the light source/videoprocessor a preliminary cleaning routine should be undertaken. Water or detergent should be sucked through the working channel in order to clear gross debris and ensure that the working channel is not blocked. This action prevents the debris from drying on surfaces and removes large numbers of microorganisms. After these steps have been completed the instrument is ready to be transferred to the processing area in an enclosed container.

Leak testing: The endoscope is detached from the light source/videoprocessor, removed to the reprocessing room and attached to a leakage tester to check the integrity of all channels before reprocessing. The leak test must be performed according to the manufacturer's instructions, in order to check the inner and outer surfaces of the endoscope for any damage. In the case of any leakage, the reprocessing procedure must be interrupted immediately and repair of the endoscope should be initiated.

Cleaning: Cleaning is a critical step that must be done properly prior to disinfection whether disinfection is performed manually or by machine. When properly done, it reduces the endoscope's bacterial load by $> 4 \log_{10}$ (99.9 percent). During this process enzymatic or non-enzymatic detergents can be used. Whilst enzymatic detergents have not been conclusively shown to be superior to other detergents in endoscope decontamination, they have the ability to digest mucus and other biological material. A fresh detergent solution should be used for each endoscope to prevent cross contamination. The detergent should be low sudsing and diluted according to the manufacturer's instructions. With manual cleaning it is important to follow the contact time, temperature and concentration recommended by the manufacturer in order to ensure a sufficient effect of the cleaning solution.

The scope should be immersed and all debris washed from its exterior by wiping and brushing. The scope should remain immersed during the cleaning process. The suction and air/water valves, the biopsy channel cover, the distal end hood, and all other removable parts should be detached while parts not intended for reuse should be discarded. Brushing should continue until there is no debris visible on the brush. All channels should be filled with detergent solution. Prolonged soaking of the channels in the cleaning solution may be beneficial if there has been a delay in initiation of the cleaning process.

Washer-disinfectors (also called automated endoscope reprocessors) have become an essential part of most endoscope reprocessing areas as they ensure a validated and standardized reprocessing cycle and also reduce staff contact with process chemicals. When using an automatic washer-disinfector it is important to be sure that

the endoscope and its components can be effectively reprocessed. Some parts (the elevator wire channel of duodenoscopes, for example) are not effectively disinfected by most models, and require manual disinfection.

High-level disinfection-sterilization: The fourth stage is high level disinfection or sterilization with a liquid chemical germicide or with one of the low temperature sterilization technics. There are many chemicals use as high-level disinfectants or sterilants in endoscope reprocessing, including glutaraldehyde, peracetic acid, hydrogen peroxide, peracetic acid/hydrogen peroxide, and orthophthalaldehyde. Disinfectant solutions may be reused; their strength should be tested by test strips to ensure the strengths remain above the minimum effective concentration. All disinfectants should be used at the correct temperature and concentration in accordance with the manufacturers' instructions. The ideal disinfectant would be:

- Effective against a wide range of organisms including blood-borne viruses.
- Compatible with endoscopes, accessories and endoscope reprocessors.
- Non-irritant and safe for users.
- Environmentally friendly for disposal.

Other factors that will influence the choice of disinfectant include the process of dilution, stability of the solution, number of reuses possible, and the cost of using the particular disinfectant.

According to the definition of EN ISO 15883, washer-disinfectors are intended to clean and disinfect medical devices, e. g. flexible endoscopes, within a closed system. Cleaning is an essential part of the reprocessing cycle. Therefore, washer disinfectors that offer the relevant cycle steps (cleaning plus disinfection plus rinse) should be recommended for use. The washer-disinfectors should fulfill the following basic criteria:

- Ensure complete irrigation of all scope channels including: biopsy, suction, air/water, auxiliary water and elevator channel.
- Avoid cross-contamination with other reprocessing batches.
- Offer a more reliable and reproducible decontamination procedure than manual processing.

- Reduce the likelihood of eye, skin and respiratory exposure

In manual disinfection the endoscope must be immersed completely. All channels must be filled with disinfectant. With manual disinfection it is important that the manufacturer's recommendations regarding correct concentration, temperature, and contact time are followed, to ensure adequate disinfection.

Rinsing: The disinfecting solution must be rinsed off from the internal and external surfaces of the endoscope. Following high-level disinfection, the scope must be rinsed with water of high microbiological purity (clean water) followed by forced air drying. Sterile water is preferable for the final rinse. The rinse water is discarded after each use.

Drying: The final step is a rinse with 70 to 80 percent isopropyl alcohol followed by a second air drying. The scope should then be dried with a soft, clean lint-free towel.

Storage: The endoscope should be hung with the tip hanging freely in a well-ventilated, dust free cabinet. Reprocessing before use does not appear to be necessary after five days of storage provided that reprocessing guidelines have been strictly observed.

Accessories: Most accessories used in the gastrointestinal tract meet the definition of critical devices and should be sterilized. Studies in

many countries have documented safe reuse of biopsy forceps, papillotomes, and argon plasma coagulator probes.

Thorough training of personnel is the first critical step in endoscope cleaning and disinfection. Staff must be properly trained and understand all aspects of handling all pieces of equipment. Each step of the decontamination cycle should be recorded, including the identity of the person undertaking each step, and this information should be linked to each individual patient examined with that endoscope.

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The Epidemiology of HIV/AIDS Infection in South Eastern European Countries

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The South Eastern European countries are on a doorway between Europe, Asia, and the African continent, a fact with potential important consequences on the epidemiology of HIV-1 infection. The duration of the HIV-1 epidemics in many countries of the region is similar to the Western Europe; however, striking differences exist in several countries of the region in both the epidemic situation and in our knowledge about it. In order to gain insight into HIV-1 diversity in the region, we reviewed the available molecular epidemiology data about HIV-1 diversity in 11 countries of the region: Albania, Bulgaria, Bosnia and Herzegovina, Croatia, Greece, Hungary, Montenegro, Romania, Serbia, Slovenia and Turkey. The existing molecular epidemiology data revealed a broad diversity in subtype distribution among countries. In several countri-

es subtype B is predominant (e.g. Serbia, Slovenia and Hungary), while in some other the proportion of non-B subtypes is much larger (e.g. Albania subtype A, Romania subtype F). In some areas, HIV-1 subtype distribution is marked by divergence between different risk groups or transmission routes (e.g. Croatia). Several major factors contribute to the breakout and spread of HIV epidemic in our area, as reflected through the process of social transition, wars, unemployment, extended drug use and high sexual risk behavior. Yet, the prevalence rate of HIV infection is low, under 0.1 percent. The set-up of a collaborative research HIV network might provide important information for better management and control of the HIV-1 epidemic in South Eastern Europe.



Status of Major Sexually Transmitted Infections in Bosnia and Herzegovina

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Objective: The aim of this paper was to review the current situation of communicable diseases surveillance particularly the laboratory based surveillance of sexually transmitted infections-STIs in Bosnia and Herzegovina.

BaH should face with significant changes in their communicable diseases surveillance system and monitoring of STIs. In terms of selecting which diseases should be included in the surveillance system is essential information on local priority diseases. No health system can undertake all communicable disease surveillance and control activities because of limited resources.

Methods: Laboratory diagnosis is mostly made using well established diagnostic systems, which is the first step leading to quality assessment. However, the possibility of getting laboratory results direct from the laboratory, promotes

self-treatment and an incorrect epidemiological situation. Short overview of the current STIs surveillance system was given as well.

Results: The task force set for communicable disease surveillance in BaH reviewed the list of priority diseases drawn up at a state-level Prioritization exercise undertaken in July 2003 in BaH. So, in the list of priority communicable diseases under surveillance in BaH are included following reportable STIs: Chlamydia trachomatis infection (genital infection); gonococcal infection; hepatitis B; HIV and syphilis.

Conclusion: Analyzing the current situation among notifiable STIs in 10-years period it is visible that serious underreporting of major STIs exists. The laboratory based surveillance should be intensified for effective control of STIs in Bosnia and Herzegovina.



Sexually Transmitted Bacterial Diseases

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Sexually transmitted diseases (STDs) are infections that you can get from having sex with someone who has the infection. The causes of STDs are bacteria, parasites and viruses. There are more than 20 types of STDs, including chlamydia, gonorrhea, herpes simplex, HIV/AIDS, syphilis, hepatitis B and C. Among them chlamydia and gonorrhea are the best known bacterial infections.

Most STDs affect both men and women, but in many cases the health problems they cause can be more severe for women. If a pregnant woman has an STD, it can cause serious health problems for the baby.

Chlamydia

Chlamydia is a common STD caused by the bacterium, *Chlamydia trachomatis*. Even though symptoms of chlamydia are usually mild or absent, can cause discharge from the penis of an infected man, serious complications that cause irreversible damage, including infertility.

Chlamydia is the most frequently reported bacterial sexually transmitted disease in the world. Under-reporting is substantial because most people with chlamydia are not aware of their infections and do not seek testing. Also, testing is not often done if patients are treated for

their symptoms. An estimated 2.8 million infections occur annually in the U.S. Women are frequently re-infected if their sex partners are not treated.

Chlamydia can be transmitted during vaginal, anal, or oral sex. Any sexually active person can be infected with chlamydia. The greater the number of sex partners, the greater the risk of infection. Because the cervix of teenage girls and young women is not fully matured and is probably more susceptible to infection, they are at particularly high risk for infection if sexually active. Since chlamydia can be transmitted by oral or anal sex, men who have sex with men are also at risk for chlamydial infection.

Chlamydia is known as a “silent” disease because the majority of infected people have no symptoms. If symptoms do occur, they usually appear within 1 to 3 weeks after exposure. In women, the bacteria initially infect the cervix and the urethra. Women who have symptoms might have an abnormal vaginal discharge or a burning sensation when urinating. If the infection spreads from the cervix to the fallopian tubes, some women still have no signs or symptoms; others have lower abdominal pain, low back pain, nausea, fever, pain during intercourse, or ble-

eding between menstrual periods. Chlamydial infection of the cervix can spread to the rectum.

Men with signs or symptoms might have a discharge from their penis or a burning sensation when urinating. Men might also have burning and itching around the opening of the penis. Pain and swelling in the testicles are uncommon.

Men or women who have receptive anal intercourse may acquire chlamydial infection in the rectum, which can cause rectal pain, discharge, or bleeding. Chlamydia can also be found in the throats of women and men having oral sex with an infected partner.

If untreated, chlamydial infections can progress to serious reproductive and other health problems with both short-term and long-term consequences. Like the disease itself, the damage that chlamydia causes is often “silent”.

In women, untreated infection can spread into the uterus or fallopian tubes and cause pelvic inflammatory disease (PID). This happens in about 10 to 15 percent of women with untreated chlamydia. Chlamydia can also cause fallopian tube infection without any symptoms. PID and “silent” infection in the upper genital tract can cause permanent damage to the fallopian tubes, uterus, and surrounding tissues. The damage can lead to chronic pelvic pain, infertility, and potentially fatal ectopic pregnancy .

To help prevent the serious consequences of chlamydia, screening at least annually for chlamydia is recommended for all sexually active women age 25 years and younger. An annual screening test also is recommended for older women with risk factors for chlamydia (a new sex partner or multiple sex partners). All pregnant women should have a screening test for chlamydia.

Complications among men are rare. Infection sometimes spreads to the epididymis, causing pain, fever, and, rarely, sterility.

Rarely, genital chlamydial infection can cause arthritis that can be accompanied by skin lesions and inflammation of the eye and urethra (Reiter's syndrome).

A single dose of azithromycin or a week of doxycycline (twice daily) are the most commonly used treatments. HIV-positive persons

with chlamydia should receive the same treatment as those who are HIV negative. All sex partners should be evaluated, tested, and treated. Persons with chlamydia should abstain from sexual intercourse for 7 days after single dose antibiotics or until completion of a 7-day course of antibiotics, to prevent spreading the infection to partners. Women whose sex partners have not been appropriately treated are at high risk for reinfection. Having multiple infections increases a woman's risk of serious reproductive health complications, including infertility. Women and men with chlamydia should be retested about three months after treatment of an initial infection, regardless of whether they believe that their sex partners were treated.

The surest way to avoid transmission of STDs is to abstain from sexual contact, or to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected. Latex male condoms, when used consistently and correctly, can reduce the risk of transmission of chlamydia.

Gonorrhea

Gonorrhea is caused by *Neisseria gonorrhoeae*, a bacterium that can grow and multiply easily in the warm, moist areas of the reproductive tract, including the cervix, uterus, and fallopian tubes in women, and in the urethra in women and men. The bacterium can also grow in the mouth, throat, eyes, and anus.

Gonorrhea is a very common infectious disease. CDC estimates that more than 700,000 persons in the U.S. get new gonorrheal infections each year. Less than half of these infections are reported to CDC. In 2009, 301, 174 cases of gonorrhea were reported to CDC.

Gonorrhea is spread through contact with the penis, vagina, mouth, or anus. Gonorrhea can also be spread from mother to baby during delivery. Any sexually active person can be infected with gonorrhea. In the United States, the highest reported rates of infection are among sexually active teenagers, young adults, and African Americans.

Some men with gonorrhea may have no symptoms at all. However, some men have signs or symptoms that appear one to fourteen days after infection. Symptoms and signs include a bur-

ning sensation when urinating, or a white, yellow, or green discharge from the penis. Sometimes men with gonorrhea get painful or swollen testicles.

In women, the symptoms of gonorrhea are often mild, but most women who are infected have no symptoms. Even when a woman has symptoms, they can be so non-specific as to be mistaken for a bladder or vaginal infection. The initial symptoms and signs in women include a painful or burning sensation when urinating, increased vaginal discharge, or vaginal bleeding between periods. Women with gonorrhea are at risk of developing serious complications from the infection, regardless of the presence or severity of symptoms.

Symptoms of rectal infection in both men and women may include discharge, anal itching, soreness, bleeding, or painful bowel movements. Rectal infection also may cause no symptoms. Infections in the throat may cause a sore throat, but usually causes no symptoms.

Untreated gonorrhea can cause serious and permanent health problems in both women and men. In women, gonorrhea is a common cause of PID. About 750,000 women each year in the United States develop PID. The symptoms may be quite mild or can be very severe and can include abdominal pain and fever. PID can lead to internal abscesses (pus-filled "pockets" that are hard to cure) and long-lasting, chronic pelvic pain. PID can damage the fallopian tubes enough to cause infertility or increase the risk of ectopic pregnancy. Ectopic pregnancy is a life-threatening condition in which a fertilized egg grows outside the uterus, usually in a fallopian tube. In men, gonorrhea can cause epididymitis, a painful condition of the ducts attached to the testicles that may lead to infertility if left untreated. Gonorrhea can spread to the blood or joints. This condition can be life threatening. In addition, people with gonorrhea can more easily contract HIV, the virus that causes AIDS. HIV-infected people with gonorrhea can transmit HIV more easily to someone else than if they did not have gonorrhea.

Specific diagnosis of infection with *N. gonorrhoeae* can be performed by testing endocervical, vaginal, urethral (men only), or urine specimens.

Culture, nucleic acid hybridization tests, and NAATs are available for the detection of genitourinary infection with *N. gonorrhoeae*. Culture and nucleic acid hybridization tests require female endocervical or male urethral swab specimens. NAATs allow testing of the widest variety of specimen types including endocervical swabs, vaginal swabs, urethral swabs (men), and urine (from both men and women), and they are FDA-cleared for use. However, product inserts for each NAAT vendor must be carefully examined, because specimen types that are FDA-cleared for use vary by test. NAAT tests are not FDA-cleared for use in the rectum, pharynx, and conjunctiva; however, some public and private laboratories have established performance specifications for using NAAT with rectal and pharyngeal swab specimens, thereby allowing results to be used for clinical management. Laboratories that establish performance specifications for the use of NAATs with nongenital specimens must ensure that specificity is not compromised by cross-reaction with nongonococcal *Neisseria* species. The sensitivity of NAATs for the detection of *N. gonorrhoeae* in genital and nongenital anatomic sites is superior to culture but varies by NAAT type.

All persons found to have who have gonorrhea also should be tested for other STDs, including chlamydia, syphilis, and HIV.

Dual Therapy for Gonococcal and Chlamydial Infections

Patients infected with *N. gonorrhoeae* frequently are coinfecting with *C. trachomatis*; this finding has led to the recommendation that patients treated for gonococcal infection also be treated routinely with a regimen that is effective against uncomplicated genital *C. trachomatis* infection. Because most gonococci in the United States are susceptible to doxycycline and azithromycin, routine cotreatment might also hinder the development of antimicrobial-resistant *N. gonorrhoeae*. Limited data suggest that dual treatment with azithromycin might enhance treatment efficacy for pharyngeal infection when using oral cephalosporins.

Antimicrobial-Resistant *N. gonorrhoeae*

Gonorrhea treatment is complicated by the ability of *N. gonorrhoeae* to develop resistance to antimicrobial therapies. Quinolone-resistant *N.*

gonorrhoeae strains are now widely disseminated throughout the United States and the world.

Decreased susceptibility of *N. gonorrhoeae* to cephalosporins and other antimicrobials is expected to continue to spread; therefore, state and local surveillance for antimicrobial resistance is crucial for guiding local therapy recommendations.

Latex condoms, when used consistently and correctly, can reduce the risk of transmission of gonorrhoea.

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Recommended Regimens

Ceftriaxone 250 mg IM in a single dose

OR, IF NOT AN OPTION

Cefixime 400 mg orally in a single dose

OR

Single-dose injectible cephalosporin regimens

PLUS

Azithromycin 1g orally in a single dose

OR

Doxycycline 100 mg orally twice a day for 7 days

Bacterial Vaginosis

Bacterial vaginosis (BV) is the name of a condition in women where the normal balance of bacteria in the vagina is disrupted and replaced by an overgrowth of certain bacteria. It is sometimes accompanied by discharge, odor, pain, itching, or burning.

Bacterial vaginosis (BV) is the most common vaginal infection in women of childbearing age. The cause of BV is not fully understood. BV is associated with an imbalance in the bacteria that are normally found in a woman's vagina. The vagina normally contains mostly "good" bacteria, and fewer "harmful" bacteria. BV develops when there is an increase in harmful bacteria.

Not much is known about how women get BV. There are many unanswered questions about the role that harmful bacteria play in causing BV. Any woman can get BV. However, some activities or behaviors can upset the normal balance of

bacteria in the vagina and put women at increased risk including: having a new sex partner or multiple sex partners, douching.

It is not clear what role sexual activity plays in the development of BV. Women do not get BV from toilet seats, bedding, swimming pools, or from touching objects around them. Women who have never had sexual intercourse may also be affected.

Women with BV may have an abnormal vaginal discharge with an unpleasant odor. Some women report a strong fish-like odor, especially after intercourse. Discharge, if present, is usually white or gray; it can be thin. Women with BV may also have burning during urination or itching around the outside of the vagina, or both. However, most women with BV report no signs or symptoms at all. BV can increase a woman's susceptibility to other STDs such as HIV, Herpes, Chlamydia, and Gonorrhoea.

In most cases, BV causes no complications. But there are some serious risks from BV including:

Having BV can increase a woman's susceptibility to HIV infection if she is exposed to the HIV virus.

Having BV increases the chances that an HIV-infected woman can pass HIV to her sex partner.

Having BV has been associated with an increase in the development of an infection following surgical procedures such as a hysterectomy or an abortion.

Preterm delivery.

BV can increase a woman's susceptibility to other STDs, such as herpes simplex virus (HSV), chlamydia, and gonorrhoea.

A health care provider must examine the vagina for signs of BV and perform laboratory tests on a sample of vaginal fluid to look for bacteria associated with BV.

Although BV will sometimes clear up without treatment, all women with symptoms of BV should be treated to avoid complications. Male partners generally do not need to be treated. However, BV may spread between female sex partners. Treatment is especially important for pregnant women. Pregnant women who have ever

had a premature delivery or low birth weight baby should be considered for a BV examination, regardless of symptoms, and should be treated if they have BV. All pregnant women who have symptoms of BV should be checked and treated.

Some physicians recommend that all women undergoing a hysterectomy or abortion be treated for BV prior to the procedure, regardless of symptoms, to reduce their risk of developing an infection.

BV is treatable with antibiotics prescribed by a health care provider. Two different antibiotics are recommended as treatment for BV: metronidazole or clindamycin. Either can be used with non-pregnant or pregnant women, but the recommended dosages differ. Women with BV who are HIV-positive should receive the same treatment as those who are HIV-negative.

Epidemiology of Urinary Tract Infections

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Epidemiology is defined as the study of the distribution and determinants of clinical states or conditions (i.e. disease, disorder, injury, harm, risk or benefit) in human populations (1-3).

More specifically, epidemiology of a clinical state should describe (descriptive epidemiology) and/or measure (analytical epidemiology):

1. Distribution of a particular clinical state in stratified populations under risk

1.1. In terms of measures of clinical state frequency

1.1.1. Rate, proportion, risk, odds, prevalence, incidence, etc.

2. Distribution of a determinant (i.e. variable associated with increased -risk factor- or decreased risk) **or a set of determinants for a particular clinical state in stratified populations under risk**

- Host determinants

- Etiological determinants (e.g. presence and characteristics of infectious agent/s, reservoir, source, vector, biogeography, etc.)

- Host-pathogen interaction

2.1. In terms of measures of association (or effect)

2.1.1. Risk ratio, odds ratio, rate ratio, prevalence ratio

3. Distribution of a marker or a set of markers of population dynamics in the course of a particular clinical state

- Direct or indirect spread (i.e. within host or population level cycles; exit, transmission, entry, invasion/dissemination, exit; biogeography)

- Individual and population level dynamics (i.e. host-pathogen interactions and variations in short- or long-term; epidemiological- or evolutionary-dynamics)

3.1. In terms of measures of infectivity, epidemics and population biology

3.1.1. Index case, primary and secondary cases, attack rate, reproductive rate, diversity indices, network indices, etc.

4. Distribution of outcomes of intervention or non-intervention in the course of a particular clinical state

- Individual- or public-level health or economic outcomes of non-intervention or different intervention modalities (i.e. in terms of outcome measures on safety, efficacy, effectiveness and value)

4.1. In terms of measures of impact

4.1.1. Morbidity, case fatality rate [lethality], mortality, absolute risk reduction, odds ratio, number needed to treat, effect size, health-related quality of life [HRQL], quality-adjusted life year [QALY], cost/billable test, cost/clinical decision, cost/intervention, interventional response time, length of stay [LOS], cost/inpatient day, cost/discharge, cost/outpatient visit, satisfaction with care, readmission rate, complication rate, etc.

Excluding genital tract infections, urinary tract infections (UTIs) are a group of clinical states or

conditions consisting of at least five distinct syndromes (i.e. uncomplicated lower UTI or cystitis, uncomplicated pyelonephritis, complicated UTI with or without pyelonephritis, urosepsis and urethritis) classified according to the predominant symptoms (4).

Although there are well studied and documented aspects of the epidemiology UTIs reliable knowledge is still lacking in certain topics whereas some features of the epidemiology is being uncovered only recently (3,5-8).

While the Cochrane Library includes 17 Cochrane systematic reviews under the “infectious diseases/urinary tract infection” category, “urinary tract infection” search term retrieves 202 and 46 hits, in any field and in title, respectively (i.e. systematic reviews, evaluations, assessments) in Centre for Reviews and Dissemination databases (CRD, including three databases: Database of Abstracts of Reviews of Effects, DARE; National Health Service Economic Evaluation Database, NHS EED; Health Technology Assessment Database, HTA: 123 + 69 + 10= 202; 28 + 13 + 10= 46). A search in Trip Database with “urinary tract infection” term retrieves 152 evidence based synopses, 177 systematic reviews, 199 guidelines, 100 core primary research, 2685 extended primary research. In PubMed Medline Database, a clinical query with the “urinary tract infection” search term retrieves 1483, 878, 1828, 1526 and 306 articles, in etiology, diagnosis, therapy, prognosis and systematic review categories, respectively.

Therefore, an attempt to describe the complete epidemiology of the five distinct syndromes included in UTIs in accordance with the above definition and in a systematic approach is an exhaustive task by scale and beyond the scope of this presentation.

Thus, this presentation will be limited to a sketchy overview of the epidemiology of UTIs (3-6,8-17).

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The Role of Microbiology Laboratory in Diagnosis and Control of Urinary Tract Infections

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Urinary tract infections (UTIs) are among the most common bacterial infections and account for a significant part of the workload in clinical microbiology laboratories.

Enteric bacteria (in particular, *Escherichia coli*) remain the most frequent cause of UTIs, although the distribution of pathogens that cause UTIs is changing. More important is the increase in resistance to some antimicrobial agents, particularly the resistance to trimethoprim-sulfamethoxazole seen in *E. coli*. Physicians distinguish UTIs from other diseases that have similar clinical presentations with use of a small number of tests, none of which, if used individually, have adequate sensitivity and specificity. Among the diagnostic tests, urinalysis is useful mainly for excluding bacteriuria. Urine culture may not be necessary as part of the evaluation of outpatients with uncomplicated UTIs, but it is necessary for outpatients who have recurrent UTIs, experience treatment failures, or have complicated UTIs, as well as for inpatients that develop UTIs.

UTIs are challenging, not only because of the large number of infections that occur each year, but also because the diagnosis of UTI is not always straightforward.

Diagnosis requires proper specimen collection, use of immediately available laboratory testing for presumptive diagnosis, and appreciation of epidemiological and host factors that may identify patients with clinically inapparent upper UTI.

Successful emergent management includes selection of appropriate antimicrobial therapy with recommendations for follow-up care. Oral therapy with an antibiotic effective against gram-negative aerobic coliform bacteria, such as *E. coli*, is the principal treatment intervention in patients with UTI (1).

UTIs have become the most common hospital-acquired infection, accounting for as many as 35-40% of nosocomial infections, and they are the second most common cause of bacteremia in hospitalized patients (2,3). The annual cost to the health care system of the United States attributable to community-acquired UTI alone is estimated to be approximately \$1.6 billion (4). Nosocomial urinary tract infections increase not only morbidity and mortality but also hospital costs.

Microbiology laboratory plays an important role in clinical practice and it is essential part of the system infection control at institutions. Effective infection control is impossible without proper microbiological support.

One of the key role of microbiology laboratory is early exposure of the pathogen on infectious diseases and especially for nosocomial infections. Therefore, it is an important that informative system of microbiology laboratory provides the information transfer of all necessary data.

For effective information system there are three main terms:

1. The confidence on quality of microbiological investigations and skills of microbiological laboratory staff to recognize pathogenic agent.

2. The capacity of epidemiologist and microbiologist to identify pseudo-outbreak and other pseudo-problems from real risks.

3. The adequate understanding by urologists the results of microbiological analysis.

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Therapeutic Challenges of Urosepsis

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INTRODUCTION

Urinary tract infections (UTIs) can manifest in a wide clinical range from bacteriuria with limited clinical symptoms to sepsis, severe sepsis or septic shock, depending on localized or systemic extension. In 20-30% of all septic patients the infectious focus is localized in the urogenital tract (1). However only 3.5% of urosepsis cases with resistant isolates in a veterans hospital occurred on the urology service (2). In one study, (3) 59 patients (54% females) with uroseptic shock were analysed over a ten year period in urology departments. Seventy-eight per cent of patients showed urinary obstruction as predisposing factors and the remaining 22% showed uropathies with a significant impact on urodynamics. Seventeen per cent of patients developed urosepsis after urological interventions. Obstructive diseases of the urinary tract leading to obstructive pyelonephritis are caused in 65% by ureteral stones, in 21% by tumours, in 5% by pregnancy, in 5% by anomalies of the urinary tract and in 4% following operations (4). In another study, from 205 analysed case histories of urosepsis, 43% resulted from urolithiasis, 25% from prostatic adenoma, 18% from urological cancer and 14% suffered other urological diseases complicated by urosepsis (5). In patients with nosocomial UTI treated in urology departments, the prevalence of urosepsis

was, on average, about 12% (6), whereas in patients with nosocomial UTI treated in other specialities the prevalence for severe sepsis was 2% and for septic shock 0.3% (7). Severe sepsis is a critical situation with a reported mortality rate ranging from 20% to 42% (8). Most severe sepsis cases reported in the literature are related to pulmonary (50%) or abdominal infections (24%), with UTIs accounting for approximately 5% (9) to 7% (10). Sepsis is commoner in men than in women (8). In recent years, the incidence of sepsis has increased (8,11), but the associated mortality has decreased suggesting improved management of patients (8,11). Urosepsis may also show high mortality rates of 25% to 60% in special patient groups (12). A consistent finding however is that the mortality associated with septic shock from a urinary source is substantially lower than all other sources. This may reflect the ease of dealing with the infected source through drainage, although this has not been established yet.

Urosepsis remains a severe situation with a mortality rate as high as 20-40%. Early recognition of the symptoms initiating rapid management of urosepsis may decrease the mortality. A comprehensive organisational structure involving urologists, intensive care specialists, radiologists, microbiologists and clinical pharmacologists, working tightly together is essential. The

prevention of urosepsis is best dependent on good practice regarding an effective and rapid management process of patients at risk.

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Prevention of Urinary Tract Infections

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Prevention of Recurrent Uncomplicated Urinary Tract Infections

Urinary tract infections (UTI) either community-acquired or nosocomially-acquired are the most common problems seen by practitioners today. Majority of community-acquired symptomatic UTI are “uncomplicated” UTI manifest in patients without structural and/or functional abnormalities or prior interventions, urethral catheterization or other instrumentation in genitourinary tract and without comorbidities that can lead to more serious outcomes. UTI are considered as “complicated” when occurring in genitourinary tracts with structural or functional abnormalities, and/or in patients underwent any instrumentation in the genitourinary tract.

Uncomplicated UTIs such as acute uncomplicated cystitis or acute uncomplicated pyelonephritis are very common among female population, accounting for more than 7 million office visits and 1 million emergency department visits in the United States annually and affecting approximately one-third of women before the age of 24 years. Moreover, these UTIs have very high recurrence rates in women, even though they are young, non-pregnant and have anatomically and physiologically normal urinary tracts. The symptoms symptoms of such UTI like painful voiding

(peeing a barbed wire), frequency and urgency significantly affect women’s quality of life, and dyspareunia (painful sexual intercourse) associated with these symptoms may lead to negative psychosexual outcomes.

In male population cystitis is uncommon in the absence of anatomic abnormality, defect in bladder emptying mechanism, or urethral catheterization. In the normal host, UTI may originate from infection of adjacent organs, usually the prostate. Nevertheless, in males aged 3 months to 50 years, incidence of UTI is low in developed countries. In developing countries the majority of UTI among young men are associated with urethritis, prostatitis or epididymitis and often transmitted in sexually manner. Older males with bladder outlet obstruction due to prostatic hyperplasia, have incomplete bladder emptying, predisposing them to UTI on the basis of residual urine. Therefore UTI in older men should be considered as complicated.

There are a great number of publications concerning preventive measures for recurrent uncomplicated UTI, varying from recommendation of food additives (such as cranberry juice) till surgical interventions (for example relocation of urethral opening in women or circumcision in men).

Non-surgical strategies to prevent recurrent UTI are listed in Table 1.

Women with high rates of UTI recurrence in relation to sexual intercourse and exposed to spermicides including nonoxynol-9, from either condoms or diaphragms, should be advised to practice alternative methods of contraception or protection from sexually transmitted diseases. Observance of sexual hygiene should also be advised.

If behavioral modifications are not sufficient other non-antimicrobial measures (see below) should be recommended, before antimicrobial prophylaxis is indicated.

Either continuous or postcoital **antimicrobial prophylaxis** with low-dose antimicrobial agents may also be effective in preventing recurrent UTI in women who suspect relation between sexual activity and subsequent manifestation of UTI symptoms. Antimicrobial agents which can be recommended for antimicrobial prophylaxis include trimethoprim or cotrimoxazole (three times a week or once daily) or nitrofurantoin (50 mg or 100 mg daily) at bedtime for 6 months and in pregnant women also oral cephalosporins, such as cefixime or cefuroxime, usually until delivery. Another alternative in women with recurrent UTI is oral fosfomycin trometamol 3 g every 10 days.

Prophylaxis should not be started until the eradication of active infection is confirmed by a

negative urine culture at least one to two weeks after the end of active treatment. Antimicrobial agents and their dosage regimen should be selected individually, considering the peculiarity of each case and the local susceptibility pattern of the uropathogens. Patients should be informed about possible adverse effects such as rash, vaginal candidosis and gastrointestinal symptoms, e.g. nausea and diarrhea.

To minimize intake of antimicrobials some patients prefer intermittent self-treatment with a short-course of antimicrobials after self-diagnosis. These patients should be carefully instructed on doses and regimen of antimicrobial course as well as symptoms and signs indicating recurrence of uncomplicated cystitis.

As a rule, before antimicrobial prophylaxis is considered non-antimicrobial measures should be recommended to minimize antimicrobial usage. However, none of these measures are effective in all patients. Unfortunately only few of them are studied in sufficiently large placebo-controlled blinded studies.

Immunoactive prophylaxis may be one appropriate non-antimicrobial option for women with recurrent uncomplicated UTI. There are number of publications on results of trials with bacterial lysates such as Uro-Vaxom, StroVac, Solco-Urovac, Urostim etc. Only Uro-Vaxom (OM-89) studied in well designed prospective, placebo-controlled trials including a sufficiently high number of patients showed a significantly reduction of new symptomatic episodes of recurrent UTI as compared to placebo by about 40%. For the other products only observational studies and case reports are available. So far there are no results of studies available comparing antimicrobial vs. immunoactive prophylaxes, which are necessary to determine the top ranking of immunoprophylaxis in the strategy to prevent recurrent uncomplicated UTI.

In postmenopausal women frequent recurrences of UTI may be related to vaginal mucosal atrophy, that leads to changes in the vaginal microflora including loss of lactobacilli and increased colonization by *E. coli*. Although oral estrogens appeared not to reduce the incidence of UTIs, local vaginal estrogens (estrogen containing creams or suppositories, estradiol-releasing

Table 1. Measures to prevent recurrent uncomplicated urinary tract infection

1a. Antimicrobial prophylaxis

- Daily/weekly reduced doses of antimicrobials
- Postcoital reduced dose of an antimicrobial
- Self short term therapy

1b. Non-antimicrobial prophylaxis

- Behavioral modifications
- Immunoprophylaxis
- Hormonal replacement (local)
- Unspecific prophylaxis (eg. urine acidification, cranberry juice)
- Probiotics

vaginal rings) seem to have a beneficial effect. Therefore, **local estriol substitution** may be one of the first line non-antimicrobial measures in postmenopausal women.

There is potential benefit of **natural products** such as cranberry juice. Studies have shown that proanthocyanidin (PAC), the active component of the juice, can inhibit bacterial attachment to the bladder and urethra. Cranberries also contain salicylic acid which by its anti-inflammatory effect may reduce urinary symptoms such as dysuria. However, salicylic acid and thus usage of fresh cranberry or cranberry juice may be contraindicated in patients with coagulation disorders and ulcers because of the risk of bleeding. Despite cranberries and cranberry products have been used widely for several decades, the available studies show conflicting results. Well designed controlled studies are required to determine the top ranking efficacy of this non-antimicrobial measure.

Another non-antimicrobial measure may be **probiotics** described as "preparations of or products containing viable, defined microorganisms in sufficient numbers, which alter the microflora in a compartment of the host and by that exert beneficial health effects in this host" (Havenaar R. and Huis In't Veld, 1992). At first the Russian scientist and Nobel laureate Eli Metchnikoff has suggested to replace harmful microbes with useful ones. Since there is a correlation between depletion of vaginal lactobacilli and increased risk of UTI, to replenish lactobacilli was suggested to restore normal vaginal flora and prevent recurrent UTIs in women. Some strains of lactobacilli, such as *L. rhamnosus* GR-1 and *L. reuteri* RC-14 have been used so far in only smaller studies (phase II). The protective effect of these probiotics is thought to include reduction of pathogen adherence, growth and colonization, and modulation of host defences. Where commercially available, it is reasonable to consider the use of intravaginal suppositories or tablets that contain *L. rhamnosus* GR-1 and *L. reuteri* RC-14 for the prevention of recurrent UTI. Use of the oral product with strains GR-1 and RC-14 is worth testing given that it can restore the vaginal lactobacilli, compete with urogenital pathogens, and prevent bacterial vaginosis, so indirectly decreasing the risk of ascending UTI. Since probiotics

are readily available without a prescription, an evidence-based review of their efficacy in the prevention of UTIs may aid consumers in making informed decisions regarding potential prophylactic therapy. Institutions and care givers also require evidence-based synopses of current evidence in order to make informed patient-care decisions.

Conclusion. Many patients, especially women are suffering on recurrent uncomplicated UTI with a great impact on quality of life. The strategy to prevent recurrent episodes include the following steps: behavioral modifications (if possible), non-antimicrobial measures and only in patients, in whom former measures were not effective, also antimicrobial prophylaxis. Because none of the measures are effective in all patients, further studies are needed for top ranking and best selection for the individual patient.

Prevention of Nosocomially Acquired Catheter Associated Urinary Tract Infections

As it was mentioned above, urinary tract infections are also the most common nosocomially acquired infections. It's related to use of urinary catheters-probably the most ancient of medical devices, having been used for centuries. It is remaining one of most needed devices in urologic practice until now. Currently, number of inserted urinary catheters is approximately 30 million per year. Being used in everyday practice, urinary catheter has merits and demerits. Main disadvantages of urinary catheter are affecting patients' quality of life and development of infectious complications.

Recent studies revealed that urinary tract infections (UTIs) are the most common nosocomially-acquired infections, accounting for approximately from 63% to 74% of all NAUTIs, and the use of urinary catheters is considered a main risk factor. In intensive care units of United States clinics 95% of UTIs are catheter-associated.

Catheter-associated urinary tract infections (CAUTIs) are the second most common cause of nosocomially acquired bloodstream infections, and each episode of symptomatic urinary tract infection additionally costs \$676, and catheter-related bacteremia is likely to cost at least \$2836.

During the last few decades, clinicians and researchers were working on development of recommendations and guidelines on prevention of CAUTIs. For this time, hundreds of scientific trials were performed on this problem. In spite of healthcare activities oriented to decreasing rates of CAUTIs, they are still high, and the problem remains of the main “pain-in-the-neck”s of urologists, nurses and intensive care unit staff. Prevention of CAUTIs is of major medical, individual and socio-economic significance, especially on account of the reduction in use of antibiotics.

The best way for CAUTIs prevention is avoid to use catheter or its remove. Therefore there are few questions which any clinician, working with catheterized patients, have to ask himself before catheterization: does this patient really need to be catheterized and if yes, how long duration of catheterization will be. During the catheterization, clinician must try to minimize urethral trauma, by the use of smallest possible catheter diameter and antiseptic lubricant jelly. Effective strategies include using of written protocols on handwashing and catheter insertion. Disposable gloves or/and sterile sleeves of the catheter (when possible) for sterile catheter insertion should be used. Hands should be washed, dried and disinfected before and after catheterization (and any manipulation of the catheter or urine drainage system). Once is placed, catheter must be removed as soon as it possible. If the patient needs a long term catheterization, then alternative methods of urine drainage such as condom catheter, suprapubic catheterization or urethral stents should be considered. Intermittent catheterization may also reduce risk of CAUTIs development. Method of urine drainage must be chosen also individually, in a glance of treatment threshold and patient's benefits. While the catheter is in place, drainage system should remain closed. Intervals of catheter change must be evaluated individually, before incrustation or obstruction of catheter occurs.

The principal cause of CAUTIs is bacterial biofilm formation by uropathogens on a catheter surface. Biofilms have major medical significan-

ce for 2 main reasons: they decrease susceptibility to antimicrobials and results of urine culture based on planctonic organisms may be false and not apply to sessile organisms living within biofilms. Many trials were performed on prevention of biofilm formation on catheter surface, such as antibiotic prophylaxis, antiseptic draining bag solutions or bladder washes, topical disinfectants, but all of this procedures lead to the same conclusion: bacteriuria and UTI can be suppressed for the short time period, but they return rapidly and eventually as resistant flora.

Using of silver-coated or antibiotic-impregnated urinary catheters may decrease the risk of biofilm formation and bacteriuria, but they as well may lead to development of silver resistant or drug resistant pathogens. Therefore, they cannot be recommended routinely. Prophylactic antimicrobial therapy to prevent infectious complications in patients with indwelling catheter is not routinely recommended, excepting cases of symptomatic UTI, urosepsis, and in patients undergoing surgical interventions and those who is at-risk for serious infectious complications. In these cases, antimicrobial treatment is optional. Other catheter care activities include washing of genitals once or twice daily with soap and water, removing of incrustations around the urethral orifice with pads soaked in antiseptic.

There elaborations on promising novel technologies such as novel biomaterials and novel coatings for urinary catheters, quorum sensing inhibitors for prevention of biofilm formation are under way, but it is too early to say about critical steps in the battle against our common enemy-nosocomially acquired catheter-associated urinary tract infections.

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Public Campaigns Aimed at Improving the Use of Antibiotics

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Public campaigns in several countries have attempted to educate the public regarding judicious outpatient antibiotic use. We retrieved information on 16 national campaigns and 6 regional campaigns (16 in Europe, 3 in North America, 2 in Oceania and 1 in Israel). All but four campaigns were conducted over more than one year (range, 1-13 years) and 12 campaigns were still ongoing in 2007. Most campaigns (n=17) were organized by health authorities and publicly funded. Two national campaigns were entirely funded by the pharmaceutical industry (Portugal, Canada). All campaigns focused on upper respiratory tract infections and used similar key messages. All but one campaign targeted physicians and the public in parallel, with an emphasis on parents of young children (n= 17). Interventions were multifaceted and varied in intensity. Distribution of information material was the most common intervention and used by all campaigns. Twelve campaigns used television

and two campaigns used intensive academic detailing for physicians. Nine campaigns observed a reduction in antibiotic prescriptions and two campaigns in self reported antibiotic use. Information on the impact of the campaigns on antimicrobial resistance, potential adverse outcomes of reduced prescribing and any sustained effects has not been published or systematically evaluated in most campaigns. In summary, public campaigns are widely used in high-income countries. Some have resulted in a reduction in antibiotic use, although a clear cause-effect relationship is difficult to establish. The lack of detailed evaluation of most campaigns, the multifaceted approach and the differences in healthcare systems make it difficult to identify the most effective interventions. Although the impact on antibiotic resistance is difficult to assess at the current moment, policy makers and epidemiologists can use our findings to develop initiatives suited to different country settings.



Effect of Governmental Policies on the Antimicrobial Use

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Antibiotics are among the most commonly used therapeutic agents. Excessive use of antibiotics is important contributor to growing worldwide antibiotic resistance. The development of new antibiotics has not kept up with the development of antibiotic resistance.

Many countries have established different activities to regulate use of antibiotics in order to prevent further increases in antibiotic resistance. Setting nationwide goals would provide policy makers and public health officials with measurable indicators to monitor progress and evaluate interventions. Responsibility of governments is to create appropriate regulations and programs to address antibiotic use and resistance. Governments, public and private institutions, and medical leaders need to implement policies and programs that encourage changes in the way antibiotics are used. Government should provide funding for public and professional education, national surveillance, research and development, and immunization, and should support international efforts to reduce antibiotic resistance. National legislative should provide that pharmacies must be managed by qualified pharmacists and have to restrict their activities to dispensing only those drugs that are directly prescribed by a qualified physician.

In addition it is necessary to establish intersectoral coordination committee with experts from various sectors. National education program should include health-care providers, veterinarians, farmers, or the general public on the appropriate use of antibiotics. Health delivery systems should routinely assess antibiotic use, and adopt policies to encourage more appropriate use. Pharmaceutical companies should voluntarily control promotional messages about antibiotics and with other stakeholders to promote prudent and correct use of antibiotics. Government should minimize marketing drugs to doctors and pharmacists. Consumer organizations should be encouraged to take up antibiotic use and resistance as consumer issues.

Conclusion: Government policies on antimicrobial use provide regulations for rationale use of antibiotics in the country, creation of national surveillance system for antibiotic resistance, monitoring prescription audits, regulatory provision for monitoring use of antibiotics in human, veterinary and industrial sectors, and identification of specific intervention measures for rational use of antibiotics.



Improving Antimicrobial Prescribing Through Knowledge, Skills and Organizational Development

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Resistance to antimicrobial agents has become a major public health problem. It is possible that we may see the return of the pre-antibiotic era if the current rate of increase in resistance to antimicrobial agents continues and the pipeline of antimicrobial drugs stays arid with the consequence that we may face a decade or longer during which introduction of new antimicrobial agents is expected to be minimal.

Thus, to ensure that options exist for treating infections, it is imperative to make the best use of those antimicrobials that are currently available. To achieve this, the Antibiotic Strategies (ABS) Project was initiated by the Austrian Ministry of Health in 1997. The objectives of the ABS Project were to analyze and to further develop the “AB culture” in Austrian hospitals, to optimize AB prophylaxis and AB therapy in the treatment of patients, and to reduce both AB resistance and the costs of AB therapy. The “Guidelines to Further Develop and Define Antibiotic Use in Hospitals” in German language in 1998 and in English in 2000 were major outputs of the ABS Project, with a revision of the German guide in 2002.

In September 2002, the project “Optimization of Antibiotic Use in Hospitals” was launched.

The objective of this project was to provide considerable assistance to Austrian hospitals in optimizing their antibiotic strategies. The programme incorporated a thorough training of the local

hospital-based antimicrobial management team, the development of local antibiotic formularies and therapy guides for the respective hospitals and the integration of the antimicrobial management team into the hospital’s organization. Counselling sessions on the implementation of the AB strategies were held in more than 30 Austrian hospitals.

After successful implementation of this programme in many Austrian hospitals an EU-funding enabled the Austrian ABS-Group to transfer this model to eight other European countries by the ABS International Project. To objectives of the ABS International Project were to analyse the ABS “maturities” of hospitals in the partner countries, to develop templates for ABS tools (surgical prophylaxis, AB therapy, ABS organization and ABS marketing), to perform a Train the ABS Trainer/ABS Consultant programme and to implement the ABS tools in cooperating hospitals by ABS training and ABS consulting. The development and validation of quality indicators for hospital AB use and the establishment of an international network of ABS experts were further valuable outcomes of this project.

After these successful projects, the “ABS Platform” was launched at the beginning of 2005 to carry on the ABS Initiative in Austria. The main activities of this platform are ABS Basic Training, ABS Advanced Training, ABS for Nurses, ABS Consulting and ABS Audits, yearly ABS Symposia and ABS research projects.

Mechanisms of Oncogenesis of Epstein-Barr Virus

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The Epstein-Barr virus (EBV) is a human herpesvirus that is a ubiquitous infectious agent, infecting greater than 90% of the world's population. The majority of infections occur early in life without significant illness. However, EBV is clearly an important factor in multiple human cancers. This dichotomy raises the question as to what are the unique aspects of infection in those who develop cancers. Many of the malignancies associated with EBV develop in the setting of immunosuppression or have endemic patterns of incidence. EBV has potent growth transforming properties *in vitro* where it efficiently induces permanent growth of infected lymphocytes. Therefore it is not surprising that EBV is clearly the etiologic factor in post-transplant lymphoma and a subset of AIDS-associated lymphomas.

The endemic patterns of incidence characteristic of many EBV-associated tumors were initially apparent as EBV was originally isolated from samples of African Burkitt's Lymphoma. EBV has also been identified in a subset of T-cell lymphomas that develop with increased frequency in Taiwan and Japan and in parotid gland tumors that occur most frequently among Inuits. The consistent detection of EBV in most Nasopharyngeal carcinoma from both endemic and non-endemic areas suggests that EBV is an essential cofactor in

the development of this tumor. Finally, there are the more recently identified tumors associated with EBV, a subset of Hodgkin's lymphoma and gastric carcinoma.

The EBV associated cancers are classic examples of the multistep nature of cancer development. The malignancies develop as a combination of a common virus with potent transforming ability, possible immune impairment, increased genetic susceptibility, in part due to HLA type, and genetic changes possibly due to environmental exposure. Potential steps in the pathway to cancer would be some event or exposure that increases the amount of virally infected cells. This might be an increase in viral replication in combination with an expanded population of a specific cell type.

However, the potent effects of EBV on cell gene expression suggest that the latently infected cells would be rapidly growing and quickly invasive. Importantly, this scenario suggests that EBV and expression of viral proteins are essential to the cancer process, to both initiation and progression. The dependence of tumor growth on viral proteins and activation of specific signaling pathways enables targeting of EBV-associated tumors through immunotherapy and specific inhibitors of activated pathways.



The Strategy for the Prevention of HPV Infection

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HPV belongs to a large family of viruses, and so far, more than 100 different types have been identified in humans. It has the highest incidence of all sexually transmitted infections and it usually occurs in young sexually active population. The two most common high-risk HPV types, 16 and 18, cause about 70% of cervical cancer cases. HPV is also associated with approximately half of vulvar and vaginal cancers, 85% of anal cancers, 36% of pharyngeal and 24% of laryngeal cancer in men and women, and 50% of cases of penile cancer. Low-risk HPV types, the most common of which are HPV 6 and 11, are associated with the development of cervical intraepithelial neoplasia (CIN 1 and some CIN 2), genital warts and recurrent respiratory papillomatosis. Although the vast majority of HPV infections are spontaneously healed, studies convincingly show that infection with high-risk HPV types are the precursors of the later development of almost all cervical cancers. Cervical cancer, as a consequence of HPV infection, is a major public health problem worldwide. Most of the European countries who, for more than 30 years have an organized cervical cancer screening based on the gynecologic examination and cervical cytology tests (Pap test), have recorded

a significant decrease in incidence and mortality rate of cervical cancer.

Prevention of HPV infection and cervical cancer in Bosnia and Herzegovina has so far been based on opportunistic screening, using conventional cervical cytology tests (cervical smear). Due to previously mentioned prevention of HPV infection, in last ten years, the number of registered invasive cervical cancer cases has decreased in Bosnia and Herzegovina, but there are still cases diagnosed in an advanced, often inoperable stage. According to the clinical stage at the moment of diagnosis, 79.65% of cases are in an inoperable stage and 27.11% of patients are under the age of 30 at the time of diagnosis.

The strategy should identify, describe and analyze new goals in public health, health care and health policy associated with HPV infection. It also suggests HPV prevention programs and strategies for the treatment of specific target groups in specialized clinics for sexually transmitted diseases, primary care centers and HIV counseling centers. Organization of the National screening programs in accordance with the latest European recommendations, introduction of new screening tests, education of patients after enlisting HPV-DNA tests into screening protocol, the

development of institutions that provide empirical basis for effective HPV and HIV testing counseling are also included in this strategy. Implementation of the modern sex education programs on responsible sexual behavior will clarify key questions about the biology, epidemiology and clinical management of HPV infections and their consequences, and thus sensitize young people and the general public about the importance of prevention, respecting all principles of human rights and ethical limits of the global stra-

tegy on prevention and control of HPV and other sexually transmitted infections. This strategy will also satisfy the educational needs of primary care physicians and other health professionals for the prevention strategy against HPV and other sexually transmitted infections. One of the strategy goals is also promoting the application of vaccines against HPV. The key role of physicians in the prevention of sexually transmitted infections should be offering available pre-exposure vaccine, as well as education and counseling.

Helicobacter and Associated Malignancy

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Helicobacter pylori has been widely recognized as a pathogen in the etiology of chronic antral gastritis and peptic ulceration. *H. pylori* is also linked to cancer and is considered to be a class I carcinogen in 1994 by the International Agency for Research on Cancer (1) and now it is considered the most common etiologic agent of infection-related cancers, which represent 5.5% of the global cancer burden (2). It induces a chronic gastric inflammation and it can play an important role in the development of gastric malignancies including gastric noncardia adenocarcinoma and mucosal-associated lymphoid tissue lymphoma (3).

It has been estimated that approximately half of the world's population is infected with *H. pylori*, and the majority of colonized individuals develop coexisting chronic inflammation. In infected subjects colonization is usually asymptomatic and tumor progression only occurs in a subset of individuals (3). However, long-term carriage of *H. pylori* significantly increases the risk of developing site-specific diseases. Among infected individuals, approximately 10% develop peptic ulcer disease, 1 to 3% develop gastric adenocarcinoma, and < 0.1% develop mucosa associated lymphoid tissue (MALT) lymphoma (4).

The role of bacterial virulence factors related to oncogenicity, host and environmental factors have been outlined to explain the oncogenesis of *H. pylori* infection in several studies and meta-analysis with scientific evidence (5-7).

Bacterial Virulence Factors

Bacterial virulence factors, such as the *cag* pathogenicity island (PAI) and cytotoxin-associated antigen A (CagA), vacuolating cytotoxin (*VacA*), outer membrane proteins (OMPs), are the most mentioned factors which are responsible for oncogenicity.

The *cag* pathogenicity island (*cag* PAI) is a 40-kb DNA insertion element which contains 27 to 31 genes flanked by 31-bp direct repeats and encodes one of the most intensely investigated *H. pylori* proteins, CagA (8). The generation of transgenic mice expressing CagA has provided more direct evidence for a causal relationship between CagA and oncogenesis by demonstrating that transgenic expression of CagA leads to gastric epithelial cell proliferation and carcinoma (9).

Approximately 60 to 70% of Western *H. pylori* strains and almost 100% of East Asian strains express CagA (10). Infection with *cagA*-positive

H. pylori strains has been associated with increased risk for development of severe gastritis, atrophic gastritis, peptic ulcer, gastric precancerous lesions, and gastric adenocarcinoma compared to those with strains that lack the *cag* island (11-14).

Homologous recombination within the 3'-region of *CagA* causes arrangement of Glu-Pro-Ile-Ala (EPIYA) amino acid containing sequences in numbers and order. Depending on surrounding sequences, the EPIYA motifs have been classified as A, B, C, and D (15). In Western strains, an increased number of *CagA* EPIYA-C sites are an important indicator of the risk of developing gastric cancer (16). The EPIYA-D motif is found almost exclusively in East Asian strains (from Japan, South Korea, and China), and strains containing this motif induce larger amounts of interleukin-8 (IL-8) from gastric epithelial cells comparing with the strains harboring Western A-B-C-type *CagA* (17).

Another virulence factor is a protein known as *VacA*, a multifunctional cytotoxin that causes intracellular vacuoles and forms membrane channels in epithelial cells (18). Polymorphisms in the signal (s), intermediate (i), and middle (m) region of *VacA* gene are associated with different disease outcome (19). In Western populations, the *vacA* s1/m1 allele is strongly associated with duodenal and gastric ulcer disease and with gastric cancer (20). East Asian strains are almost all *vacA* s1/m1 and, as predicted, are not associated with any specific clinical outcome (5).

Outer membrane proteins of *H. pylori* are important for binding to gastric epithelial cells and are essential for colonization and chronic persistence, which can affect clinical outcome. The blood group antigen binding adhesin (*BabA*), and the sialic acid binding adhesin (*SabA*) have been identified as major outer membrane proteins that bind to Lewis b antigen and related sialyl-Lewis x and sialyl-Lewis a antigens, respectively (21). The presence of *babA2* is associated with duodenal ulcer disease and gastric cancer, and when found in conjunction with *cagA* and *vacA* s1 alleles, it is associated with an even greater risk of developing more severe disease. Geographic origin of *H. pylori* strains are shown to be important in the clinical outcome of the disease. In Portuguese and Thai populations, *babA2*

is not a biomarker for peptic ulcer disease or gastric cancer. However, for strains isolated from Germany, Turkey, or northern Portugal, *babA2* expression is associated with the severity of gastric disease (5).

Outer inflammatory protein (*OipA*) is an inflammation-related outer membrane protein (22). *H. pylori* contains either a functional or nonfunctional *oipA* gene, and the presence of a functional gene is significantly associated with the presence of duodenal ulcers, gastric cancer, and increased neutrophil infiltration (23).

H. pylori-induced epigenetic alternation, including DNA methylation and histone modification, as well as its interaction with gastric stem cells or progenitor cells are important topics that will greatly enhance our understanding of the bacteria-induced carcinogenesis; therefore, they are currently the target of extensive investigation (24).

Host Factors

H. pylori infection induces chronic inflammation and expression of a variety of cytokines. Genetic polymorphisms in cytokine-encoding genes may affect the magnitude and type of the response. Polymorphisms in tumor necrosis factor- α , IL-1, IL-6, IL-8, IL-10, TLR-4, COX-2, glutathione S transferase (GST), Toll-like receptor, mannose binding lectins and HLA have also been associated with increased risk for gastric cancer, gastric lymphoma and pre-neoplastic lesions (25,26).

Environmental Factors

The risk of gastric adenocarcinoma is influenced by environmental elements as well. High dietary salt intake has been shown to be associated with an increased risk of gastric cancer some prospective studies (27,28).

On the other hand, dietary influences especially the abundance of foods rich in antioxidant micronutrients decrease gastric cancer risk. The possible influence of diet in determining oncogenicity of *H. pylori* is suggested by recent work demonstrating that high salt concentrations lead to higher expression of *CagA* (27-29).

Coinfection with helminths may have an impact on the outcome of *H. pylori* infection. In a study of Colombian children, where a higher

Th2-associated IgG1 response was reported for children infected with both helminths and *H. pylori* and living in a coastal region where the incidence of gastric cancer is low (30).

Cigarette smoking in combination with infection by *H. pylori* CagA⁺ strains was also found to increase the risk of developing gastric cancer in German, Japanese and Swedish populations (5).

Not only gastric malignancies but also extra-gastric some other cancers have been mentioned in the patients infected with *H. pylori*. The association between presence of *H. pylori* and pancreatic cancer, esophageal cancer and hepatocellular carcinoma has been also reported (31,32). People infected with *H. pylori* appeared to be at high risk of pancreatic cancer. An association has also been reported between *H. pylori* infection and pancreatic cancer. A meta-analysis of 7 studies quantified to 65% the increased risk of pancreatic cancer in people infected with *H. pylori* (31). In esophageal cancer it has been suggested that infection with *H. pylori* is protective to adenocarcinoma, but might be a risk factor for squamous cell carcinoma, although the role of *H. pylori* in the etiology of these cancers remains somewhat unclear (33).

It is apparent from recent studies that cancer risk is the summation of the polymorphic nature of the bacterial population in the host, the host genotype, and environmental exposures, each affecting the level of long-term interactions between *H. pylori* and humans. It is important to gain more insight into the pathogenesis of *H. pylori*-induced gastric adenocarcinoma, not only to develop more effective treatments for this common cancer but also because it might serve as a paradigm for the role of chronic inflammation in the genesis of other malignancies that arise within the gastrointestinal tract.

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Viral Hepatitis and Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world. Over 80% of cases are related to viral hepatitis. Up to 80% of HCC in Southeast Asian countries are related to hepatitis B (HBV) infection. Hepatitis C (HCV) is the most important cause of HCC in Japan, Europe and North America, where HCV antibodies can be detected in up to 70% of patients with HCC. In the majority of cases, there is underlying liver cirrhosis.

In HBV infected patients with cirrhosis, the annual risk of developing HCC is estimated at 2.2 and 3.7% in Caucasians and Asians, respectively. Among HCV infected patients with cirrhosis, the rate is 1-4% per year.

HBV can integrate into the human genome and influences the carcinogenesis by cis- and transactivation pathways, as well as indirectly by necro-inflammatory and regeneration injury. Virological factors such as high viral load, genotype C and basal core mutations have been described to be associated with increased risk of malignant transformation.

Hepatitis C virus does not integrate into the host genome. HCV contributes to hepatocarcinogenesis predominantly through indirect pathways, but it may alter lipid metabolism and signal trans-

duction pathways via its structural and nonstructural proteins. Among chronic hepatitis C patients, HCC only develops in the presence of advanced liver fibrosis or cirrhosis. HCV genotype and HCV-RNA level do not influence the rate of fibrosis progression or the risk of HCC development.

The most effective measure of prevention of HBV-related HCC is prevention of HBV infection by vaccination. A universal vaccination program in Taiwan was shown effective in reducing the rate of childhood and early adulthood HCC.

The ability of antiviral agents to prevent HCC in patients with chronic HBV infection is controversial. Interferon-alfa therapy appears to be effective in preventing HCC in cirrhosis in Asia but not in Europe. Medium-term nucleos(tide)-analogue therapy significantly reduces but does not eliminate the risk of HCC, especially in patients with pre-existing cirrhosis. Maintenance of virological remission is important for the reduction of HCC risk. With more potent antiviral drugs currently available (entecavir, tenofovir), long-term HBV-DNA suppression is now possible with very low risk of drug resistance. There is no clear evidence that anti-HBV therapy reduces the rates of recurrence in patients treated with hepatic resection or local ablation of a HCC.

There is also limited evidence for a reduction of the risk of HCC in patients with chronic HCV achieving sustained viral response (SVR) including cirrhotic patients, mainly because of the short follow-up of patients with chronic hepatitis who have higher rates of SVR and the least risk of developing HCC. Interferon has also been employed in the tertiary prevention of HCC in HCV patients treated with hepatic resection or

tumor ablation. A meta-analysis of 5 controlled studies could not demonstrate any tertiary prevention, mainly as a consequence of inadequate design and conduct of the studies.

Continued HCC surveillance, especially in cirrhotic patients, under nucleos(t)ide analogues for chronic hepatitis B and, even after sustained viral response, for hepatitis C, is recommended.



HCV Treatment: Where Do We Stand?

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Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide, which affects 3% of world population. The long-term consequences are variable, from mild hepatitis to extensive fibrosis, cirrhosis and hepatocellular carcinoma (HCC). Chronic hepatitis is a silent disease, so most of the patients are unaware of the infection. On the other hand in 20-40% of patients mode of transmission remains unknown. Treatment of chronic hepatitis C has advanced in recent decade as a result of modern developments in diagnostic and therapeutic possibilities. The primary goal of HCV treatment is eradication of infection, which is defined as undetectable HCV-RNA 24 weeks after the cessation of treatment, which is defined as sustained virologic response (SVR). SVR is generally associated with resolution of liver disease in patients with mild to moderate fibrosis. Patients with cirrhosis remain at risk for HCC and have to be monitored even after achieving SVR.

Standard-of-care (SoC) for patients with chronic hepatitis C is combination of pegylated interferon (IFN)- α and ribavirin in duration according to genotype. Both pegylated interferons α (2a and 2b) are considered equally effective in elimination of HCV. SVR rates for genotype 1 patients in European population are about 50%, while in genotypes 2 and 3, 5 and 6 elimination of HCV can be achieved in 80% of patients.

The results of therapy for genotype 4 are slightly better than in genotype 1.

The strongest predictors of SVR are the genetic polymorphism of IL28B (or IFN λ 3) gene, HCV genotype and the stage of fibrosis.

Response-guided therapy according to viral kinetics viral load and fibrosis can improve the eradication rates for 10-15%. Correction of cofactors (body weight, alcohol consumption), administration of supportive therapy, as well as adherence to full doses of pegylated interferon as well as ribavirin can further improve the success rates. New therapeutic strategies, especially direct acting antiviral drugs, aim toward higher SVR rates, shortened treatment and easier administration. Triple therapies including two NS3/4 protease inhibitors, boceprevir and telaprevir in combination with pegylated interferon and ribavirin are likely to be approved by the EMA and FDA in late 2011. Both of those therapies should increase SVR rates in naïve and non-responder patients. The future developments aim at triple direct antiviral drug treatment that would completely avoid interferon and inhibit the emergence of resistant HCV strains, similar to current HIV treatment. However it will probably take a decade until this goal is reached.



Treatment of HBV

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Hepatitis B virus (HBV) infection is a health care problem all over the world. There has been a significant paradigm change of its treatment in the last decade. Treatment of HBeAg-positive and -negative patients generally aims at long-term suppression of the replication of the virus, although the ultimate goal is HBsAg seroconversion. Conventional interferon is replaced by pegylated interferon. It provides HBeAg seroconversion in nearly 1/3 of HBeAg-positive patients. Lamivudine is an L-nucleoside, being the first antiviral drug for HBV treatment. Its use is limited by a significantly high rate of resistance. Telbivudine, another L-nucleoside is more potent than lamivudine. However it has also a resistance rate of 10-20% after 2-year use. Adefovir is a nucleotide analogue and has weak antiviral activity. It is effective against nucleoside-resistant mutations. Long-term emergence of resistance also limits the use of adefovir beside its nephrotoxicity. Recently two antivirals are developed:

entecavir and tenofovir. Entecavir, a cyclopentane is very potent: after 5 years nearly 95% of the patients have undetectable HBeAg-DNA. Resistance develops in 1.2% of previously untreated cases although lamivudine-resistant patients develop entecavir resistance in rate of 50% in 5 years. Tenofovir, another nucleotide analogue, is less nephrotoxic and more potent than adefovir. It is effective against both treatment-naive and treatment-experienced patients. No resistance has been defined after its use of 3-5 years. The antiviral drugs demonstrated benefits including histologic improvement, HBeAg seroconversion, HBV-DNA suppression, and ALT normalization. The availability of potent, less toxic antivirals provided long-term suppression of HBV-DNA and possibly less complications of HBV infection including cirrhosis and hepatocellular carcinoma. The challenge is appropriate use of these drugs to minimize the antiviral resistance and maintain optimal HBV-DNA suppression.

Microbiological Diagnosis of Viral Hepatitis

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Viral hepatitis is caused by hepatitis viruses A, B, C, D, and E. Of all these viruses only hepatitis B virus (HBV) belongs to the DNA viruses, all the other ones [hepatitis A virus (HAV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV)] included in the RNA viruses. Methods used in order to diagnose hepatitis viruses basically may be divided into two groups:

1. Indirect methods: Test methods based on determination of antibodies against hepatitis viruses from the serum or plasma samples by using the most frequently enzyme immunoassay (EIA), enzyme linked immunosorbent assay (ELISA) or chemiluminescence methods (CLIA) may be evaluated in this group.

2. Direct methods: Determination and quantification of DNA or RNA material belonging to the investigated hepatitis virus from serum, liver tissue or stool samples—only for HAV—by using the most frequently and widely used nucleic acid tests (NAT) based on amplification of the target region such as polymerase chain reaction (PCR), reverse transcriptase-PCR (RT-PCR), real time-PCR (rt-PCR) transcription mediated amplification (TMA) and reverse-hybridization methods or signal amplification: branch-DNA (b-DNA) in

routine diagnostic laboratory procedures. Direct Sequencing of DNA or RNA materials of the hepatitis viruses, genotyping tests and HCV Core antigen test, specifically used in order to diagnose and confirm HCV infections, also included in this group.

Since HCV had never been visualized and grown in cell culture and natural viral proteins were unlikely obtained, laboratory diagnosis of the HCV viruses have still many problems. So that reason it may be getting more and more important day by day to establish accurate diagnostic procedures especially for HCV infections for routine laboratories. Diagnostic tests of HCV may be divided into three groups:

1. Screening test (anti-HCV tests based on EIA or CLIA)

2. Supplemental test (recombinant immunoblot assay-RIBA)

3. Confirmatory test (HCV RNA or a new and automated HCV Core Ag test, may be included in this group as a second line confirmatory test).

The most common problem in the laboratory screening assay of anti-HCV is the false positivity of low titers. Among immunocompetent populations with anti-HCV prevalence less than 10%

(e.g., volunteer blood donors, health care workers,...etc) the proportion of false positive results averages approximately 35% (range: 15% to 60%). Among immunocompromised populations (e.g., hemodialysis patients) average rate of false-positive results approximately: 15%.

Although third-generation HCV reactivities are more sensitive and specific than older generation assays, they still have a high percentage of false positive reactions, so that it is mandatory to confirm every reactivity, especially with low titers by

anti-HCV CIA or EIA with HCV RNA assay (lower limit of detection: 50 IU/mL or less) or with newly developed and automated HCV Core Ag test -as a secondary confirmation test- to avoid false positive results. Many studies concluded that HCV Core Ag test showed good performance and correlation with HCV-RNA for diagnosis of HCV (patients at pre-seroconversion period and low risk group blood donors) and monitoring to response to antiviral therapy.



Imaging in Chronic Hepatitis and in Its Complications

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In this speech, following questions will be answered:

1. Which radiological modality is the best for diagnosing of chronic viral hepatitis?;
2. Could liver fibrosis be diagnosed noninvasively?;
3. What can we do when an incidental liver lesion is found on radiological methods in a chronic hepatitis patient?;
4. Could a lesion be characterized in a chronic hepatitis patient? and How? (advantages and

disadvantages of radiological methods and differences among contrast materials);

5. Which radiological interventional methods are present to treat a liver tumor (from percutaneous alcohol ablations to Yttrium-90 radioembolizations)?

Also, the questions will be answered about the appropriate radiological screening modality and screening time. On this manner, many radiological cases will be presented.



Management of HCV Infection in Drug Users: Experiences from Slovenia

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The prevalence of HCV infection in 2 million population of Slovenia has been estimated below 0.5% which is in accordance to the prevalence reported from some other Middle European countries. Hepatitis C is predominantly managed by the infectologists whereas severe complications are taken care by gastroenterologists-hepatologists. In 1997 an interdisciplinary Slovenian Hepatitis C Study Group was set-up with the purpose to rationalise the management of HCV infection in Slovenia according to the internationally recommended standards yet taken into account national particularities.

In 18 centres for prevention and treatment of drug addiction managing approximately 3000 drug addicts the prevalence of anti-HCV among 1450 tested was 30% whereas the prevalence of HCV RNA was 15.6% compared to 50-60% at the beginning of nineties when the first testing was performed. To improve the detection of HCV infected drug users, their further follow up and treatment at viral hepatitis centres, the Slovenian National Consensus Guidelines for the Management of Hepatitis C Virus Infection in Drug Users have been set up in 2007. They comprise practical step-wise diagnostic and therapeutic procedures as well as strategy oriented towards improvement in screening for HCV infection, highly qualified education and counselling, better epidemiological surveillance and as much as possible treatment of hepatitis C according to individual evaluation of infected drug addict. A national healthcare network for the complex management of HCV infected drug users

was established combining the drug addiction and viral hepatitis centres. It consists of addiction therapists, viral hepatitis specialists, virologist, sub-specialized psychiatrists/therapists and councilors. There is also a peer-lead team that supports patients either personally or on-line and other supporting system consisting mainly of family members, friends and co-workers. The interdisciplinary team receives special medical as well as supportive education through various means including annual interdisciplinary conferences.

Since 1997 the treatment of patients with chronic hepatitis C in Slovenia has been followed up systematically on the national basis. Three prospective national multicenter studies on efficacy and safety of currently recommended standard of care regimens (standard interferon alpha monotherapy, standard interferon alpha plus ribavirin, pegylated interferon alpha plus ribavirin) in intent to treat patients have been performed so far, the fourth (optimized pegylated interferon alpha plus ribavirin) not being completed yet. The proportion of drug users included into the intent to treat hepatitis C treatment regimens has been increasing over the last 14 years, from 5% between the years 1997-1999 to even 66% in the last few years. Interestingly, in the last completed study with over a third of drug users participating, only 7% of all the treated patients discontinued the treatment due to non-compliance whereas the proportion of successfully treated naive patients has been in accordance to the results of pivotal international clinical trials.

Treatment of Meningitis with Multidrug Resistant Bacteria

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Introduction: Nosocomial meningitis represents serious problem in Neurosurgery and Infectious diseases. It is characterized by distinctive features in clinical presentation, etiology and treatment.

Objective: To analyze presence of nosocomial meningitis confirmed etiologically with in vitro resistance to traditional antimicrobials and possibility of their treatment.

Patients and methods: Retrospective analysis of medical histories of neurosurgical patients diagnosed with meningitis caused by multidrug resistant bacteria had been conducted. Patients were hospitalized at Clinic for Neurosurgery for the past two years. Diagnosis was established based on two of four possible criteria: clinical, pleocytosis above 20 cells with polymorphonuclear predominance, hypoglycorrhachia and confirmation by positive liquor culture and antibiogram.

Results and discussion: We noticed shift in antimicrobial spectrum of causative agents from gram-positive to gram-negative bacteria. Incre-

ased presence of *Acinetobacter* spp. was noted compared to *Pseudomonas aeruginosa* and *Enterobacteriaceae*. In gram-positive spectrum staphylococcus was predominant. After analyzing antibiograms we noticed that listed hospital pathogens are becoming more resistant to traditional antibiotics. Also, treatment is complicated with patients allergic to sensitive antibiotic or group of antibiotics. We implied all of the above as meningitis caused by multiple drug resistant bacteria when we resorted to usage of old untraditional antibiotics or new ones with lack of personal clinical experience or those who are not registered for this indication or administration. We emphasized combined treatment and alternative ways of medicament administration.

Conclusion: Our experiences correlate with available literature.



Current Trends in Beta-Lactamases and Interpretation of Antimicrobial Test Results

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In *Enterobacteriaceae* the most common beta-lactam resistance mechanism, is the production of beta-lactamases that inactivate the antibiotic. Four major groups of beta-lactamases can be identified based on their substrate specificities: penicillinases, AmpC-type cephalosporinases, extended spectrum beta-lactamases (ESBLs) and carbapenemases. There are currently more than 900 beta-lactamases listed in the Lahey site (www.lahey.org/Studies).

ESBLs are serine beta-lactamases that belong to the group 2be of beta-lactamases according to the Bush-Jacoby-Mederios classification. ESBLs hydrolyze all beta-lactams except cephamycins and carbapenems. Their activity is inhibited by beta-lactamase-inhibitors such as clavulanic acid, sulbactam and tazobactam although the efficacy of the inhibitors may differ between the types. ESBLs were first described in 1983 in Germany among *Klebsiella* spp. and soon become a major problem worldwide. Until recently, ESBLs mostly belonged to the TEM and SHV families and were considered as a problem of hospitalized patients. In recent years, however, there were considerable changes in the epidemiology of the ESBLs which can be summarized as the worldwi-

de emergence and spread of CTX-M enzymes in the hospital and in the community.

CTX-M enzymes are now considered as the most prevalent enzymes in *Enterobacteriaceae* and commonly found in *K. pneumoniae*, *E. coli*, *Salmonella* spp., *Shigella*, *Enterobacter* spp., *Citrobacter freundii* and *Serratia*. These enzymes are plasmid-borne and usually connected with IS elements such as ISCR1 and ISEcp1 which enhances their mobilization. It was demonstrated that certain clones such as ciprofloxacin resistant *E. coli* 025:H4-ST131 have the ability to acquire multiple resistance plasmids along with CTX-Ms. Dissemination of this clone is particularly important in community-acquired UTIs and has been detected in several European countries and also in Turkey

*bla*_{CTX-M} genes are usually located on large plasmids which concomitantly carries other resistance genes such as other ESBLs (up to 5), plasmid-mediated quinolone resistance genes (qnr A-D, aac(6') Ib-cr, qep and oqx) and plasmid mediated 16srRNA modifying enzymes (rmt A-D, armA) which confer aminoglycoside resistance.

The new danger that has turned into a global crisis is the dissemination of carbapenemase production among *Enterobacteriaceae* especially in *K. pneumoniae* and *E. coli*.

In gram-negative bacteria, two groups of beta-lactamases confer resistance to carbapenems: those that have serine at the active site (serine carbapenemases) and which could further be classified as class A (KPC, GES, etc) and class D (OXA-carbapenemases) and those that use a Zn^{+2} ion (metallo beta-lactamases; MBLs). Among serine carbapenemases the most important are the *K. pneumoniae* carbapenemases (KPCs). There are currently 11 variants, KPC-2 being the most common. With the aid of plasmids, bla_{KPCs} have spread among the *Enterobacteriaceae* and non-fermentative bacteria and has become endemic throughout the world.

Oxacillinases that exhibit carbapenemase activity are often found in *Acinetobacter* spp. In recent years however, these enzymes (particularly OXA-48) are increasingly reported in *Enterobacteriaceae* in particular *K. pneumoniae*. In a recent SENTRY study that analysed carbapenemase production in *E. coli* and *K. pneumoniae* isolated in 2007-2009, OXA-48 producing isolates were detected in Turkey in all years and in Argentina in 2007 and 2008. The number of OXA-48 producers in Turkish hospitals increased from 2 in 2007 to 27 isolates in 2009.

MBLs are found globally in numerous species. Most of them (75%) are plasmid mediated and thus transferable. The major families include VIM and IMP beta-lactamases which are originally identified in *P. aeruginosa* but now spread to *Enterobacteriaceae*. An increasing concern is the rapid spread of a novel MBL originated from New Delhi, India and named NDM-1. NDM-1 was originally identified in a *K. pneumoniae* isolate which caused UTI in a Swedish patient in 2008 but spread to other *Enterobacteriaceae* and also recently to *A. baumannii*. As NDM-1 gene is very mobile, it moved from India and Pakistan to UK, USA, Kenya, Japan, Canada, Belgium, Netherlands, Finland, Taiwan, Singapore and Australia.

Carbapenemases are really worrisome as KPCs and MBLs virtually hydrolyse all beta-lactams leaving colistin and tigecycline as last resorts.

Detection of ESBLs and carbapenemases could be challenging for routine laboratories although it is a must for infection control and patient management. In 2010 and 2011 however CLSI and EUCAST changed recommendations concerning the detection and reporting of these beta-lactamases based on pharmacokinetic/pharmacodynamic data. In summary, resistance categories should be determined by using new breakpoints and should be reported as seen. Screening and confirmation tests should be done if asked for and for infection control only. Although this approach seems to confer to reporting susceptibility results without delay, time will show the effects on patient management.

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Interpretation and Clinical Aspects of AST Results

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CASE 1

- Female, 45 years old
- Fever, epigastric pain, nausea
- 7 days later, admission to emergency dep. with fever, confusion & hipotension
- Colesistectomy in previous month

CASE 1

- Temp.: 38.3°C Blood P.: 80/40 mmHg
- Pulse: 96/min. Respiration R :20/min.
- Hb: 11 g/dl
- WBC: 14.500/mm³
- Differential: 85 % neutrophil, 7% band, 7% lymphocyte

CASE 1

Abdominal CT → Liver mass (10 cm Ø)



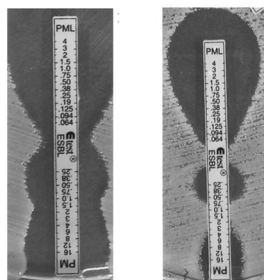
Interventional radiology → Aspiration material
→ Culture

CASE 1

Isolate: K.pneumoniae

Ampicillin	S
Ampicillin/Sulbactam	S
Ceftriaxone	S
Ceftazidime	I
Cefepime	S
Aztreonam	S
Gentamicin	S
Imipenem	S
Ciprofloxacin	S
TMP/SXT	I

CASE 1



CASE 1

CLSI ESBL Detection ??

CASE 2

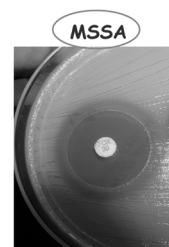
Male, 52 years old, chronic eczema
 cefazolin, oral ampicillin, flucloxacillin
 → for infected eczema
 At admission ;
 Temp.: 39°C Blood P.: 95/55 mmHg
 Left leg:
 eczema lesion + cellulitis

CASE 2

Culture: *S. aureus*

AST

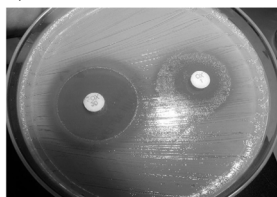
Penicillin	R
Erithromycin	S
Clindamycin	S
TMP/SXT	S
Ciprofloxacin	S
Fusidic acid	S
Vancomycin	S



Cefoxitin 30 µg - 26 mm

CASE 2

Parenteral flucloxacillin started
 → No improvement at day 4
 Repeat test for methicillin resistance



FOX - 25 mm S
 OX - 12 mm I
 OX - MIK = 4µg

CASE 2

Community acquired MRSA ?
 5th day -
 i.v vancomycin + rifampin
 ↓
 9th day - fever, shivering, hypotension, hemoptysis
 Chest X-ray → Small, fluid containing cavities
 Tomography → Numerous abscesses

CASE 2

- PBP2a (latex) - Negative
- *mecA* PCR - Negative

FOX - 25 mm S
 OX - 12 mm I
 OX - MIK = 4µg

CASE 2

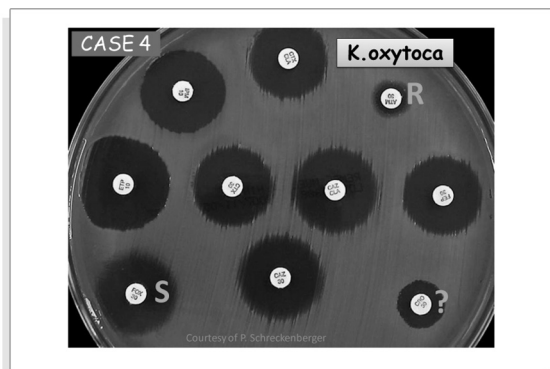
How would you interpret the lab. results with the clinical course ?



CASE 3

Direct reading of the E. cloacae isolate is given. How should it be reported?

Ampicillin- R	Ampicillin-
Cefazolin- R	Cefazolin-
Ceftazidime- I	Ceftazidime-
Cefepime- S	Cefepime-
Ceftriaxone- S	Ceftriaxone-
Gentamicin- S	Gentamicin-
Amikacin- S	Amikacin-
Levofloxacin- S	Levofloxacin-



CASE 4

Automated System Results

Types:	Gram Negative General Susceptibility 143 (GNS-143)		
Status:	Final		
Elapsed Time:	7 hours		
Organism:	Klebsiella oxytoca		
Sources:	Manual		
	MIC	Instrument	Expert
Ampicillin	>=32	R	
Ampicillin/Sulbactam	>=32	R	
Piperacillin/Tazobactam	>=128	R	
Cefazolin	>=32	R	
Ceftriaxone	<=8	S	
Ceftazidime	<=8	S	
Cefepime	<=4	S	
Aztreonam	>=32	R	
Imipenem	<=4	S	
Gentamicin	>=16	R	
Tobramycin	8	I	
Ciprofloxacin	<=0.5	S	
Levofloxacin	2	S	
Trimeth-sulfa	<=10	S	
Nitrofurantoin	<=32	S	
ESBL			Positive

MIC values in mcg/ml (M) Wait for All

CASE 4
Which phenotypic feature does not fit with the ESBL (+) result of the automated system?

CASE 4
What can be the resistance mechanism in *K. oxytoca*?

CASE 4
How should this *K. oxytoca* isolate be reported?

CASE 5
Klebsiella pneumoniae isolate in urine culture of a catheterized afebrile patient >100,000 cfu/mL

CASE 5

CXM- R
 CAZ- R
 CRO- R
 CTX- R
 FOX- R
 FEP- R
 PIP- R
 TZP- R
 IMP- S

CASE 5
Automated System Results

Type: Gram Negative General Susceptibility 143 (GNS-143)
 Status: Final
 Elapsed Time: 13 hours
 Organism: *Klebsiella pneumoniae*
 Source: ID Rate (665473631)

	MIC	Instrument	Expert
Ampicillin	>=32	R	
Ampicillin/Sulbactam	>=32	R	
Piperacillin/Tazobactam	>=128	R	
Cefazolin	>=32	R	
Ceftriaxone	>=64	R	
Ceftazidime	>=32	R	
Cefepime	>=32	R	
Meropenem	>=64	R	
Imipenem	<=4	S	
Gentamicin	>=16	R	
Tobramycin	>=16	R	
Ciprofloxacin	>=4	R	
Levofloxacin	>=8	R	
Trimeth-sulfa	>=320	R	
Moxifloxacin	>=128	R	
ESBL			Negative

MIC values in mcg/ml (MI) Wait for All

CASE 5

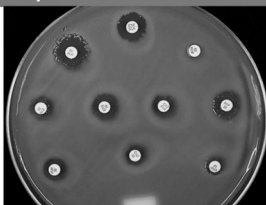
Type: Gram Negative General Susceptibility 143 (GNS-143)
 Status: Final
 Elapsed Time: 13 hours
 Organism: *Klebsiella pneumoniae*
 Source: ID Rate (665473631)

Only IMP-S
 ESBL (-)
K. pneumoniae

CASE 5
What is the next step ?

CASE 5

What is the most probable resistance mechanism in this *K. pneumoniae* isolate?





Molecular Diagnosis of Zoonosis

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Molecular tools have been used for various purposes in zoonotic infections. They are preferred for their high sensitivity and accuracy, different level of specificity, rapidity and ability for differentiating in species for better characterization of zoonotic transmission. They have been also used increasingly in taxonomy of some zoonotic infections. Utility of molecular tools in zoonotic infections can be summarized as follows:

1. Diagnostic purposes: Molecular tools have been facilitating a sensitive, rapid detection for many zoonotic agents at species, subspecies, and genotype levels in various specimens. The conventional approaches such as, microscopy, culture, and serological methods have limited sensitivity for detecting low level infections whereas molecular tests can help to detect low level of agents in clinical specimens especially at the beginning or late stage of the infection. Their detection limit can be as low as 10 copies RNA/DNA if sample collection, transportation and processing procedure are well coordinated. This is crucially important to identify asymptomatic carriers and latent or recrudescing infections. In addition, molecular methods can also give an opportunity retrospective analysis of zoonotic infections during the treatment stage of patients.

2. Identification, re-identification/reclassification of zoonotic agents: Molecular tools have dramatically changed our understanding of the epidemiology of several zoonotic diseases. For instance, the new etiological agents have been identified and some old classifications have also been revised. Incidence of the zoonosis in a region, country, and all over the world has been updated. Since clinical and geographic distribution of species or subspecies in the same genus can be different, accurate species/subspecies identification has critically important. For instance; molecular tools can differentiate *Francisella* species into four subspecies of which, *F. tularensis* subsp. *tularensis* is the most virulent in humans and found in North America. However, *F. tularensis* subsp. *holartica* was found in North America, Europe, and Asia. Polymerase chain reaction (PCR) and sequencing can help us to identify, re-identify and reclassify some specific zoonosis. Based on 16S rRNA gene sequence, *Ehrlichia equi* was reclassified as *Anaplasma phagocytophilum*, and more than 22 species or subspecies were determined in *Bartonella* genus. A multiplex PCR can identify *Brucella* isolates at species level.

3. Molecular epidemiology: In the presence of conventional epidemiological data, molecular typing methods provide very useful data about

transmission dynamics of zoonotic agents. Molecular typing results can prove cross-transmission, transmission route, transmission degree and contamination sources. Molecular tools can distinguish out-breaks from sporadic or unrelated endemic cases. These tools may also serve to identify multiple episodes in a specific host, differentiate new episodes of infection from re-activation of latent infection. For instance the use of multiple-locus variable-number tandem repeat analysis (MLVA)-16 typing for *Brucella* species makes possible to confirm relapses, laboratory-acquired brucellosis, or intra-familial brucellosis. MLVA-25 typing of *Bacillus anthracis* isolates identifies clonal relationship among the isolates from animals, environment and humans. As a result of this, the transmission route, degree, and period among different sources can be estimated. Moreover, it can be possible to identify predominant genetic clones in a population, region, and country or all over the world.

4. Determine drug resistance: Molecular tools have been used widely for detection of mutations responsible for drug resistance in several viral, parasitic, and bacterial zoonosis. Especially in viral infections, molecular tests give more rapid, sensitive and accurate results for drug resis-

tance both in treatment-naive patients or patients already on treatment. For instance, PCR and sequencing can identify amino acid substitutions in the transmembrane domain of M2 protein (positions 26, 27,30, 31, or 34) which confer resistance to amantadine in Influenza A viruses. Pyrosequencing is an easy technique to detect base substitution at 275 nucleotide position in neuraminidase gene of pandemic influenza A H1N1 (2009) viruses responsible for oseltamivir resistance.

5. Characterization of pathobiology of zoonotic diseases: Molecular tools can be used to understand the reasons of various clinical presentations of a specific etiological agent in different hosts. Detailed molecular analysis can identify variation in virulence of the pathogens in species, subspecies or genotype levels. They have enhanced the understanding of the pathogenicity, virulence, and host-parasite relationships of the etiological agent. For instance, molecular researches showed that host genetics is an important determinant of the intensity of infection and morbidity due to human helminthes. For instance, only 10-30% of people exposed to infection will develop alveolar echinococcosis.



Clinical and Epidemiological Characteristics of Brucellosis

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Aim: To analyze the frequency and distribution of human brucellosis in the Federation of Bosnia and Herzegovina (FBiH) in the period 2001-2010, and clinical and epidemiological characteristics of hospitalized patients with brucellosis.

Method: In this descriptive, retrospective study, we used official reports in infectious diseases from public health institutes of FBiH. The clinical and epidemiological characteristics of brucellosis were retrospectively analysed in 176 patients hospitalised in the Clinic for Infectious Diseases Tuzla from January 1st 2000 to December 31, 2010. The diagnosis of brucellosis was confirmed by positive results of blood culture and/or by serology testing.

Results: In the period 2001-2010, there were 2174 human brucellosis cases. In that period in the Clinic for Infectious Diseases Tuzla were hospitalised 176 patients with human brucellosis. 164 (93.1%) were inhabitants of rural regions.

Average age of patients was 40.6 years. Males were significantly often infected (79.5%). Patients were mostly hospitalized during spring season. Contact with infected animals was registered in 83.4% of patients. The leading symptoms and signs of the disease were fever, arthralgias, weakness, night sweating, headache, anorexia, hepatosplenomegaly. Complications were documented in 18.1% of males and 2.2% of females. Relapse of the disease was registered in 14.2% of patients. Chronic brucellosis was developed in 5.1% of patients.

Conclusion: Brucellosis is a very serious problem for Bosnia and Herzegovina. Controlling brucellosis requires planning at the national level, better cooperation between the veterinary and health sectors, financial resources, and health education for health professionals, veterinarian professionals, and the general population.



Brucellosis-an Overview of the Treatment Experiences by the Mostar

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Brucellosis is a zoonosis with a world-wide distribution, which is becoming increasingly more frequent in Bosnia and Herzegovina. Although it has very important medical meaning in the entire Mediterranean basin, a unique treatment scheme is still lacking. One of the possible reasons for such situation is the discrepancy between antibiotic sensitivity when analysed in the in vitro and in vivo situations. The central question for the treatment analyses is the necessity for any antibiotic to be effective at the fagosome level in the sufficient concentration, much greater than its minimum inhibitory concentration.

The current experiences suggest that using a single antibiotic to treat brucellosis should be avoided, suggesting that the use of two or even more agents might provide better treatment outcomes. The paper also describes the specificities of some localised forms of the diseases, such as endocarditis, should be combined with occasional surgical procedures, also ensuring better treatment outcomes. The paper discusses the main treatment dilemmas, as well as the effectiveness of the treatment based on the recurring diseases frequency, post-treatment sequellae and the possible existence of chronic forms of the disease.

Candida Infections in Patients with Hematologic Malignancies

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Fungal infections are an important cause of morbidity and mortality in patients with hematologic malignancies. Prolonged neutropenia, impaired cell-mediated immunity, and fungal colonization after the administration of broad-spectrum antibiotics are known predisposing factors. Patients with hematologic malignancies are predisposed to invasive fungal infections because of the immune suppression that accompanies the disease process and its treatment. The rate of candida infections is declining, it is still a major concern, especially among high-risk populations such as cancer patients. Candida species are the most frequent cause of invasive fungal infections in neutropenic patients. Although *C. albicans* is the most common cause of candidemia, there has been a shift to non-*albicans* species in recent years. Candidiasis is a spectrum of infections that may be cutaneous, mucosal, or deeply invasive. Deeply invasive infections include candidemia, disseminated candidiasis, or single-organ candidiasis. Common risk factors for candidiasis in neutropenic patients include extended duration of neutropenia, mucosal disruption of the gastrointestinal tract caused by cytotoxic chemotherapy, presence of intravascular catheters, repeated courses of broad-spectrum antibiotics, the use of potent immunosuppressive regimens such as corticosteroids and colonization. Invasive mycotic infections are a growing problem, especially in the settings of criti-

cal care and compromised immune function. The percentage of patients who develop invasive fungal infections (IFI) has increased dramatically in recent decades. Most of these infections occur in patients with hematologic malignancies.

Candida species are the most frequent cause of invasive fungal infections in hematologic malignancies. Although *C. albicans* is the most common cause of candidemia, there has been a shift to non-*albicans* species in recent years. *Candida glabrata* is an increasing cause of candidemia, especially at cancer centers.

Our data of candidemia among hematology/oncology patients during 2006-2011 *C. albicans* was the most common isolate, accounting for 55.19% of the candida isolates. However, the proportion of non-*albicans* species was 44.81%. Our study among hematology/oncology patients during 2005-2011 year founded that *C. albicans* was the most common candida species caused candidemia (55.19%), than *C. glabrata* (26.78%), *C. tropicalis* (8.74%), *C. krusei* (6.56%), *C. kefyr* (1.64%) *C. parapsilosis* (1.09%). In patients with neutropenia, it appears that the gastrointestinal tract is the most common source of candidemia, making catheter removal or exchange less likely to be as effective. Strategies to prevent fungal infections include those aimed at decreasing fungal colonization and those aimed at augmenting the host's immune response.

Trends in Antifungal Resistance Among *Candida* spp.

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Over the last 20 years, candida species have become prominent nosocomial pathogens. Infections due to candida species are associated with increased mortality and morbidity, longer duration of hospital stay and increased costs. *Candida* spp. have been reported to be the fourth commonly isolated microorganism from nosocomial bloodstream infections with a highest mortality rate. Rapid initiation of appropriate antifungal therapy is essential for the management of candida infections. This should be directed by the species identification of the organism and the local epidemiology of these infections including the antifungal susceptibility patterns.

More than 90% of invasive infections due to *Candida* spp. are attributed to five species—*C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis* and *C. krusei*. Although *C. albicans* has been reported to be the most common etiologic agent, reports have documented a shift from *C. albicans* as the cause of majority of invasive infections toward non-*C. albicans* species, especially species such as *C. glabrata*, *C. krusei*, *C. parapsilosis* which are less susceptible or resistant to the main antifungal agents being used for the treatment. Widespread use of antifungals due to the increase of candida infections among immunocompromised and intensive care patients resulted in antifungal resistance in candida species.

Most species are susceptible to amphotericin B. Resistance to amphotericin B is rare in *C. albicans* isolates. Amphotericin B resistance is innate or due to phenotype switching upon exposure to the drug in *C. lusitaniae*. Amphotericin B resistance has been reported in *C. glabrata*, *C. guilliermondii* and *C. rugosa* isolates. Fluconazole is another widely used antifungal drug and fluconazole resistance among isolates of *C. albicans* (0.8-1.5%), *C. tropicalis* (3-6.6%), *C. parapsilosis* (2-4.2%), *C. lusitaniae* (1.6-6.6%), *C. kefyr* (0-5.7%) has remained infrequent worldwide between 1997 and 2003. Elevated rates of resistance (6.3-66%) have been reported among isolates of *C. glabrata*, *C. guilliermondii*, *C. rugosa* and *C. famata*. *C. glabrata* is a focus of concern regarding fluconazole resistance. *C. inconspicua* and *C. norvegensis* have been described as species of candida with reduced susceptibility to fluconazole. Cross resistance between fluconazole and extended spectrum triazoles is well described for *C. glabrata* however it is uncommon with *C. krusei* which is intrinsically resistant to fluconazole. Also *C. guilliermondii*, *C. inconspicua* and *C. norvegensis* appear to be susceptible to voriconazole while *C. rugosa* appears to be resistant to voriconazole as well as fluconazole. Echinocandins show excellent activity for *C. albicans*, *C. glabrata*, *C. tropicalis* however elevated MICs were ob-

served for *C. parapsilosis* and *C. guilliermondii*. Echinocandins have been reported to be active against fluconazole resistant strains of *C. rugosa* and *C. inconspicua*.⁵ Flucytosine resistance has been documented to be 0-0.6% for *C. albicans* and 0.6-6% for all candida species combined.

In conclusion we can say that antifungal resistance is not as alarming as antibacterial resistance among candida species however some species and isolates show high levels of resistance to specific antifungals so antifungal susceptibility patterns should be followed closely.



Aspergillosis in a Patient with Neutropenia

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Invasive infections caused by fungi aspergillus are a major cause of morbidity and mortality in immunosuppressed patients (transplant recipients, AIDS, hematologic malignancies, chronic corticosteroid therapy, chronic granulomatous disease). In recent years aspergillus and aspergillosis have been a major focus of clinical mycology because the number of patients with this disease has risen dramatically and because of the difficulty in diagnosing and treating invasive infection. The spectrum of clinical syndromes associated with aspergillosis is diverse, ranging from allergic response to the organism, asymptomatic colonization, superficial infection, and acute or subacute invasive disease. Invasive aspergillosis most heavily affects lungs and central nervous system. Affection of sinuses or disseminated form of invasive aspergillosis is seen less often. Among numerous aspergillus species (more than 250 species in 7 subgenera and in multiple sections), invasive aspergillosis is mostly caused by *A. fumigatus*, *A. flavus*, *A. niger* and *A. nidulans*. Species identification of an aspergillus species has become important because differences in antifungal drug susceptibility and likely pathogenicity may be identified. *A. nidulans*, for example, has been reported as a cause of infection in patient with chronic granulomatous disease

and is a species that may be resistant to amphotericin B. Risk factor for developing of invasive aspergillosis is neutropenia (risk of 5-25%), with higher risk if it lasts for longer than 3 weeks and with lower cell number. A proven diagnosis of invasive aspergillosis requires a tissue biopsy showing invasion with hyphae and a positive culture for aspergillus. Detection of galactomannan by EIA has contributed substantially to the diagnosis of invasive aspergillosis. Molecular diagnosis including polymerase chain reaction have also been developed for aspergillus but these assays are not standardized and remain investigational, although this approach is very promising for improving the diagnosis of invasive aspergillosis. Historical efficacy of antifungal therapy in invasive aspergillosis has been extremely poor, with favorable responses in less than 40% of patients, and overall mortality rates are almost 60%. Response to antifungal therapy depends on several factors, including the immune status of the host and the extent of infection at time of diagnosis. A prompt diagnosis and effective initial therapy are both critical in improving the outcome of this infection. Voriconazole is a potent, broad-spectrum triazole that has become the recommended primary therapy for most patients with invasive aspergillosis. The drug can be given orally or intravenously and at the same dose

sage. In one randomized trial, comparing voriconazole and amphotericin B deoxycholate, voriconazole was successful in 52% of patients as compared with only 31% in those receiving amphotericin B deoxycholate. Superiority of voriconazole was demonstrated in patients at high risk for mortality, including those undergoing bone marrow transplantation and in those with extrapulmonary disease, including cerebral aspergillosis. For more than four decades amphotericin B deoxycholate has been the gold standard therapy for critically ill patients with invasive asper-

gillosis. However, several recent studies have consistently documented the limited efficacy and substantial toxicity of amphotericin B deoxycholate in high-risk patients. The overall response rates of amphotericin B deoxycholate are less than 25%, with responses of only 10-15% in more severely immunosuppressed patients. Additional antifungal agents are lipid amphotericin formulations, other triazole antifungals (itraconazole, posaconazole, isavuconazole) and echinocandins (caspofungin, micafungin, and anidulafungin).



MDR, XDR and PDR Superbugs: Global Threats

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Pandrug-resistant (PDR), extensively drug-resistant (XDR), and multidrug-resistant (MDR) gram-negative bacilli (GNB) are designated as those resistant to all, resistant to all but one or two, and resistant to ≥ 3 classes of antimicrobial agents, respectively. XDRGNB of clinical importance include *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia* and other glucose-non-fermentative GNB. Risk factors for colonization or infection with XDR superbugs include critically-ill patients with prolonged length of hospitalization, exposure to an intensive care unit, receipt of mechanical ventilation, exposure to a variety of broad-spectrum antibiotics, recent surgery, invasive procedures, and underlying severity of illness. Infections caused by these XDRGNB consist of hospital-acquired pneumonia, ventilator-associated pneumonia, intraabdo-

minal infections, and catheter-related bacteraemia. In addition, these superbugs are also considered as colonizers in various body sites, particularly in respiratory tract. Combination therapy with at least one in vitro active agents for invasive XDRGNB infections is usually recommended. Tigecycline (*K. pneumoniae* and *A. baumannii*), polymyxin B or E (colistin) (*P. aeruginosa* and *A. baumannii*), and sulbactam or rifampin (*A. baumannii*) in combination with other agents are promising options, although clinical evidence for these treatment regimens is limited. The discovery of new drugs active against hospital-acquired XDRGNB infections to prevent a future medical and social catastrophe is ongoing. In the interim, appropriate use of currently available antibiotics (use of antibiotics with less collateral damages) and strict adherence of adequate infection control policy are crucial.



PK-PD on Antibacterial Resistance

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Whereas infections caused by multidrug-resistant microorganisms are increasing worldwide, there are few new antibiotics, preclinical and clinical development. There are extensive data showing that the administration of antimicrobials according to pharmacokinetic/pharmacodynamic parameters improves the possibility of a positive clinical outcome, particularly in severely ill patients.

Evidence is now accumulating (both experimental and clinical) that the application of pharmacokinetic/pharmacodynamic principles can also help control antimicrobial resistance by avoiding the exposure of microorganisms to antimicrobial doses that exert selective pressure rather than eradicate them.

The three main pharmacokinetic/pharmacodynamic parameters able to predict antimicro-

bial efficacy are the maximum concentration (C_{\max})/minimum inhibitory concentration (MIC) ratio, the area under the concentration-time curve (AUC/MIC) ratio and the time during which the drug concentration exceeds the MIC ($T > \text{MIC}$). The relative importance of the three pharmacokinetic/pharmacodynamic parameters varies according to different antimicrobial classes, and sometimes overlaps.

This presentation will summarize the most significant experimental and clinical data on the optimization of the use of antimicrobials according to pharmacokinetic/pharmacodynamic parameters, in an effort to improve patient care and limit the development of pathogen resistance to available drugs by achieving optimal antimicrobial exposure at the infection site.

Laboratory Detection of Extended-Spectrum Beta-Lactamases

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Extended-spectrum beta-lactamase (ESBL) are a group of enzymes that are capable of hydrolysis of cephalosporins of the first, second and third generations and aztreonam (but not cephamycine and carbapenems), sensitive to their inhibitors such as clavulonic acid sulbaktam and tazobactam. They represent an impressive example of the ability of gram-negative rod bacteria to develop mechanisms of resistance to antibacterial drugs opposed to the introduction of new antimicrobial drugs. Classification of beta-lactamases are based on their functional characteristics (A, B, C and D class) or the primary structure (group I, II, III, IV).

Laboratory diagnostics of ESBLs is based on applying phenotypic and genotypic testing methods examination as recommended by the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M100-S20 Vol.30 No 1 NCCLS/CLSI or European Committee on antimicrobial susceptibility testing (EUCAST) Version of 1.3, January 5, 2011. As an initial screening tests for detection of ESBLs there are recommended disk diffusion and broth microdilution methods measuring the inhibition zone on third generation cephalosporin's, cephamycin and monobactams or growth in a specific concentration of the same antibacterial drugs. The increase in inhibition of the zone diameter ≥ 5 mm of any an-

tibiotic that has been tested in combination with clavulonic acid in relation to the diameter of the zone of the same antibiotic alone is a confirmation of ESBL producer, or a reduction in MIC values ≥ 3 double concentration of any antibiotic tested in combination with clavulonic acid compared to the value of MIC of the same antibiotic alone also confirms the presence of ESBL producer.

Phenotypic detection of chromosomally encoded AmpC beta-lactamases is based on proving the resistance of some isolates to penicillins, third generation cephalosporin's and cephamycins but sensitivity on cloxacilins, oxacilins, and aztreonam, or appears as blunted ends between clavulanic acid and third cephalosporin's generations. Antagonism in the form blunt ends between the cefoxitin and oxyiminocephalosporins and monobactams, suggests the production of inducible AmpC beta-lactamase. Plasmidal encoded AmpC beta-lactamases we can detect using the AmpC disk test, where is disk impregnated with Tris-EDTA. The test is positive if inhibition zone between cefoxitin and AmpC disk is like indetation or flattening, which indicates enzymatic inactivation of cefoxitin (positive result), or test is negative if the absence of a distortion is indicating no significant inactivation of cefoxitin.

Detection of metallo beta-lactamase-carbapenemase we base on susceptibility testing of isolates to meropenem, imipenem and ertapenemu by usage of disk diffusion test or microdilution test. If *Enterobacteriaceae* are resistant to one or more members of the cephalosporin subclasses III (cefoperazone, cefotaksim, ceftazidime, ceftizoxime and ceftriaxone) and that show elevated MICs or reduced zone diameters of carbapenems with positive modified Hodge test that confirms the presence of carbapenemase.

Tracking the origin and movement of nosocomial infections is not possible without developed molecular methods for detection and typing of certain ESBL. Until today numerous molecular

methods are described such as PFGE, multiplex-PCR and DNA sequencing or pyrosequencing. One of the very fast, reliable and sensitive molecular tests that can detect within 7 to 8 hours of most ESBLs, carbapenemase and AmpC beta-lactamase is Check MDR-CT101 and Check MDR-CT 102 (Check-Points com). This test can be of real ESBLs variants separating from non-ESBL subclasses TEM and SHV-wild type. By application of molecular methods it is possible to avoid certain disadvantages of phenotypic methods of detection and one of the most important benefits of detecting type of resistance in isolates from two phenotypic profiles which have large clinical and epidemiological benefits.

Treatment Approach to Multidrug Resistant Bacterial Infections

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Antibiotics which are chemotherapeutic agents that inhibit or abolish the growth of microorganisms, such as bacteria, fungi, or protozoans, are developed to kill the microorganisms. Microorganisms develop and disseminate resistance as an opposite reaction to antimicrobials in accordance with the rules of the physics, evolution and natural selection. In spite of considerable developments in the antibiotics, antibiotherapy, science, medicine and medical care, infectious diseases and infectious complications related to resistant bacteria such as staphylococci, respiratory pathogens including gram-negative bacilli, fungi and viruses remain as an important cause of human morbidity and mortality. In the first decade of the third millenium, methicillin-resistant *Staphylococcus aureus* and coagulase-negative staphylococci (MRSA), extended-spectrum beta-lactamase (ESBL) positive and/or carbapenem resistant *Enterobacteriaceae*, multidrug-resistant or pandrug resistant *Pseudomonas* spp. and *Acinetobacter* spp. remain as the major multidrug-resistant microorganisms that infectious diseases physicians face.

Treatment Approach in MRSA Infections

The major options in the treatment of MRSA infections are vancomycin, teicoplanin linezolid,

daptomycin, tigecycline and quinopristin/dalfopristin. Ceftobiprole and ceftaroline are also new cephalosporin agents. Vancomycin may be a suitable alternative in cases with a minimum inhibitory concentration of 1 mg/L or less. Linezolid is effective in the treatment of pneumonia and meningitis due to its favorable pharmacokinetics to these sites. Daptomycin is effective in the treatment of bacteremia and endocarditis. Rifampin may be added in difficult to treat infections such as meningitis and osteomyelitis. Fucidic acid and fosfomycin may be used in salvage therapy in some cases.

Treatment Approach in ESBL Producers

ESBL-producer gram-negatives are a worldwide problem. In cystitis fosfomycin, nitrofurantoin and temocillin may be considered due to favorable in vitro susceptibility data clinical efficacy. In addition klavulnic acid + oral third generation cephalosporins, co-trimoxazole, co-amoxiclav and ciprofloxacin may be used in susceptible strains. In systemic infections carbapenems are the the main options. In intraabdominal and complicated soft tissue infections tigecycline may be considered.

Treatment Approach to Multidrug Resistant or Pandrug Resistant *Pseudomonas* spp. and *Acinetobacter* spp.

There is no consensus choice in the treatment of MDR *Pseudomonas* spp. and *Acinetobacter* spp. infections. Treatment should be tailored according to the antibiotic susceptibility patterns of the strains. In case of susceptibility carbapenems and colistin are the main options. In acinetobacter infections tigecycline, colistin and sulbactam are the major options.

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New Identification Methods for Old Pathogens

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The typing of pathogenic bacteria from patients, in food and water for human consumption, and in environmental samples is part of the much larger process of diagnostic and public health microbiology. With the advent of genomic analysis new methods for antigen and nucleic acid detection are now possible and are being developed. To maximise the benefit to all from these “new generation” tests they must be linked to the identification and typing of isolates for clinical and epidemiological purpose as well as to the evolutionary biology of the pathogenic process. With the new data rich genomic based techniques we can improve our ability to do this by developing schemes which will create natural groupings of genetically related isolates. This should allow a rapid and definitive identification (within currently used, and so recognisable, nomenclature) and could also provide a measure of the relatedness of two strains; a label far more informative to epidemiologists than “indistinguishable” or “closely related”. The data generated

from such typing schemes are numeric in nature, portable and relatively easy to standardise; the opportunity therefore exists for truly global investigations which can be carried out in both developed and developing country laboratories and could be used routinely to track outbreaks caused by international travel from a single location or globally distributed food stuffs. In the longer term it should be possible to recognise genetic elements associated with outbreak, or successful, strains and so inform basic science in way which facilitates the development of early warning systems. To be fully unlocked deployment of appropriate techniques for typing is necessary at the local level. *Salmonella enterica* is a very good example of a globally relevant pathogen where this process is underway. The use of Multi Locus Sequence Typing (MLST), to define serotypes, followed by SNP (single nucleotide polymorphism) typing, or MLVA (Multi Locus VNTR analysis), for fine resolution, could eventually replace current methods.



Travel Associated Diarrhea

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The increasing number of people travelling internationally has given birth to a new medical discipline: the travel medicine. Particularly relevant are the health risks involved in traveling to and from developing countries; almost 50% of travelers develop some sort of health complication after such a journey.

Travelers' diarrhea (TD) is among these infectious diseases that many are exposed to. It is a self-limited illness that affects around 6 million people a year, and increased incidence rates of TD have remained high for the last 50 years.

In the history of TD, the consumption of food, particularly unpasteurized dairy products, raw or undercooked meat and shellfish, as well as beverages contaminated with fecal matter may be crucial.

Bacteria are the predominant agents of infection, and one of the most common causes of TD

is enterotoxigenic *E. coli* (ETEC), however the enteropathogens that cause TD vary geographically around the world. Enteraggregative *E. coli* (EAEC) is a recently emerging bacteria, especially in Central America. In some regions of the developing world, *Campylobacter jejuni* is a common cause of TD. More rare causes of TD include other bacteria such as *Shigella*, *Salmonella*, and other pathogenic *E. coli* and protozoan such as *Giardia*. Viruses are less common causes of TD than bacteria.

Many causes of TD have no microorganisms identified as a cause.

Some pathogens are more likely to cause disease during certain seasons.

Options for prevention include travelers' education and eventually a chemoprophylaxis.



Clostridium Infection in Hospitalized Patients: Diagnosis and Molecular Epidemiology

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Clostridium difficile infections (CDI) are usually recognized as toxin-mediated antibiotic-associated diarrhea, colitis or pseudomembranous colitis commonly related to health-care facilities and elderly patients. *C. difficile* which is the leading cause of hospital-associated diarrhea is however changing its epidemiology since rate of CDI is showing an increasing trend in previously low-risk populations.

Since 2002 increasing rates of *C. difficile* have been reported from USA and Canada, mostly associated with the emergence of a particular strain known as PCR ribotype 027 (BI/NAP1/027: restriction endonuclease analysis group BI; North American pulsed-field type 1; ribotype 027). In Europe health-care associated ribotype 027 epidemics have been recognized starting from the year 2005. This particular ribotype besides the usual toxins A and B, produces a binary toxin with yet an unknown mechanism of action. The strain is characterized as toxinotype III and had a deletion in *tcdC* gene which is a negative regulator for the production of toxins A and B and also another deletion at 117. position leading to the formation of a truncated TcdC protein. These two molecular properties lead to the

production of more toxin and increase the severity of CDI.

In Europe first multicenter study about health-care associated CDI was done by European Study Group of *C. difficile* (ESGCD) in 2002 in 8 European countries and later in 2005 in 14 European countries. These studies revealed more than 66 different PCR ribotypes mainly ribotype 001, 014. Ribotype 027 was found in 6% of the toxinogenic isolates. Following October 2003 large outbreaks caused by ribotype 027 have been reported from United Kingdom. In 2007 36% of all *C. difficile* cases in United Kingdom were found to be ribotype 027, followed by 106 and 001. The European-wide analysis performed in 2007 revealed that ribotype 027 had affected health-care facilities in 11 European Union countries while this number increased to 16 countries in 2008. Increasing resistance to macrolides, clindamycin and fluoroquinolones for *C. difficile* ribotype 027 isolates may aid to the persistence and spread of these strains.

The study planned by ECDC in 34 European countries in November 2008 indicated 64 different *C. difficile* ribotypes, among which ribotypes 014/020, 001 and 078 were predominating

whereas the prevalence of 027 was 5%. It was concluded in this survey that the incidence of CDI varied between countries and was higher than documented in 2005.

C. difficile ribotype 027 has also been detected in Japan first in 2007. Surveillance studies in Asian countries indicated that ribotype 017 is more frequently encountered in Asia than other countries. Toxin A⁻ toxin B⁺ *C. difficile* strains also increased in incidence in South Korea and ribotype 027 was first described in 2009. Except for one case of 027 reported from Hong Kong in 2009, most of the *C. difficile* isolates in China were ribotype 017.

Few reports from Latin America revealed the isolation of *C. difficile* ribotypes 106 and 017. However, these data were not later supported by using highly discriminative MLVA (multilocus variable-number tandem-repeat analysis) technique. No data exist for *C. difficile* infection incidence or characteristics in Africa and only few reports indicated presence of *C. difficile* isolates in Middle East.

Community acquired *C. difficile* infection incidence is also increasing recently. Patients with community acquired CDI are usually younger than health-care associated ones and the related ribotypes are generally different than the ribotypes isolated from hospital associated cases. Since ribotypes in the community seem to differ from those in the hospitals, *C. difficile* pressure from hospitals to the community is still a matter of debate. Animals seem to be candidates for a community reservoir through their feces or contaminated meat, since *C. difficile* may be a commensal and a pathogen in animals and farm animals which are often exposed to antibiotics.

Laboratory Diagnosis of *C. difficile* Infections

The proper management of patients with CDI is mainly based on rapid and accurate laboratory diagnosis. Proper laboratory testing of *C. difficile* requires good specimen collection, rapid transport and prompt handling in the laboratory. There are many variabilities and shortcomings of methods used in laboratory diagnosis of *C. difficile*.

Diagnostic approaches for *C. difficile* can be classified as “non-molecular” and “molecular” methods. Among the non-molecular methods

there are enzyme immuno assays, cell cytotoxicity neutralisation assay (CCNA), anaerobic toxigenic culture (TC) and glutamate dehydrogenase (GDH) antigen detection. Molecular methods are based on nucleic acid amplification techniques. IDSA and SHEA guidelines on diagnostic testing of CDI recommend testing only on diarrheal stool and indicate toxigenic culture (TC) as the most sensitive method. However, it is well-known that TC is not practical for routine diagnosis. They also recommend a two-step algorithm using glutamate dehydrogenase (GDH) antigen detection followed by toxin testing.

The most common laboratory test used to diagnose CDI is an enzyme immunoassay (EIA) to detect *C. difficile* toxins A and/or B. However, that these tests generally have suboptimal sensitivity and specificity especially in areas of low prevalence. Thus, it has been recommended that EIAs should not be used routinely as a single test for the diagnosis of CDI.

Cell cytotoxicity neutralisation assay (CCNA) relies on the detection of a cytopathic effect in cell culture that is neutralised by the presence of antibodies to *C. difficile* toxins. CCNA requires the ability to perform cell culture which requires a degree of expertise. Toxigenic culture (TC) relies on the anaerobic culture of *C. difficile* from stool samples. Following growth and identification of *C. difficile* on CCFA (cycloserine cefoxitin fructose agar), the isolates are later confirmed for the production of toxin either by CCNA or PCR. While CCNA detects the presence of *C. difficile* toxins, TC detects *C. difficile* bacteria or spores that have the potential to produce toxin. Thus, a faecal sample may be CCNA negative but TC positive and a TC-positive result does not always indicate CDI. Therefore these two methods are usually considered as reference methods pointing out two different targets. TC identifies patients who have the potential to develop *C. difficile* diarrhea. On the other hand CCNA is a better test for the laboratory confirmation of CDI. As expected TC is more sensitive than CCNA.

Glutamate dehydrogenase (GDH) which is a common antigen of *C. difficile*, is used as a marker for the presence of *C. difficile* in stool. Seve-

ral authors recommend a two-step algorithm using GDH as an initial screening test. Since GDH detects both toxigenic and non-toxigenic strains of *C. difficile*, it must be followed by a toxin detection assay such as EIA, CCNA or PCR.

Accurate diagnosis of CDI is vital for patient management, infection control and for reliable surveillance data. Two-step algorithms with prudent test selection according to the local needs and resources of each laboratory seem to perform better for the diagnosis of CDI.

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Enteric Pathogens in Patients with Diarrhea

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Diarrhea is a syndrome that can be caused by infectious and noninfectious agents. Globally, there are about two billion cases of diarrheal disease every year. Diarrheal diseases can be community-acquired, hospital-acquired, acquired during travel or persistent in normal and compromised hosts.

The main infectious etiology of the diarrhea is related to a wide range of bacteria (such as, *Shigella* spp., *Salmonella* spp., *E. coli* and *Vibrio cholerae*) entero-parasites (*Giardia* spp. and *Entamoeba histolytica*), and viruses (rotavirus, adenovirus and Norwalk virus). In general, the same pathogens are responsible for diarrhea worldwide, with only variations in the frequency of occurrence of each pathogen in different localities. The most identified enteric pathogens are salmonella and campylobacter, but many of the poten-

tially important agents are not detectable by means of routine diagnostic laboratory tests; (enterotoxigenic *E. coli*, enteroaggregative *E. coli*, enteroinvasive *E. coli*, noncholeraic vibrios, and noroviruses).

Studies of enteric pathogens and their toxin are important for determining the mechanisms by which they cause disease and spread throughout a population. Some bacteria produce secretory enterotoxins that invade cells directly, but others invade cells or produce cytotoxins that damage cells or trigger host response. Viruses and protozoa disrupt cell functions and cause short or long-term disease.

In controlling diarrheal disease it is important to establish national and international network for epidemiological and microbiological surveillance patients and food.



Molecular Epidemiology of *Acinetobacter*

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Acinetobacter is a gram-negative, glucose non-fermenting bacterium emerging worldwide in hospitals as an opportunistic pathogen with multi-drug resistance phenotype. The taxonomy of acinetobacter is highly complex which divided this bacterium to genospecies based on DNA-DNA hybridization and 16s RNA typing. Genomic species II, also named as *Acinetobacter baumannii* is the most significant genospecies causing serious infections in hospitals especially in

intensive care units. PCR typing, ribotyping, pulse field gel electrophoresis (PFGE) and multi-locus sequence typing (MLST) are the methods used in molecular epidemiology of *A. baumannii*. Among these, PFGE and MLST are preferred as being more robust and reproducible. In this presentation we will discuss the applications of these molecular methods, their advantages and disadvantages to each other and the epidemiology of *A. baumannii*.



Management of Multidrug Resistant *Acinetobacter baumannii* Infections

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Acinetobacter species are non-fermenting aerobic gram-negative, non-spore forming and oxidase negative cocobacillary. Despite the low-virulence of this microorganism, it is an emerging pathogen in hospitals. The ability to survive under a wide range of environmental conditions, to persist for extended periods of time on surfaces, to cause outbreaks of infection, to be endemic in hospitals, the capacity for extensive antimicrobial resistance and the potential for airborne spread make it an important pathogen in hospitals, especially in intensive care units. It causes a wide range of infections, including bacteremia, pneumonia, meningitis, urinary tract infection and wound infection. The frequency of multi-drug resistance (MDR) is increasing in many health-care settings and treatment of these infections becomes problematic. The risk factors for MDR-*A. baumannii* are prolonged length of hospital stay, exposure to an intensive care unit, support with mechanical ventilation, previous administration of antibiotics, recent surgery, performance of invasive procedures and presence of severe illness. The organism cause outbreaks in hospital settings due to environmental contamination and hand contamination of health-care workers. Colonisation of the inanimate hospital environment is of great importance for the trans-

mission of MDR *A. baumannii*. The associated crude mortality is ranging from 26% to 68%. The extent of antimicrobial resistance, the effectiveness of empirical therapy and the availability of definitive therapeutic options effect the outcomes. It is difficult to say that the attributable mortality of these infections independent of patients' severe underlying disease. Certain patient characteristics (age, immunosuppression, recent surgery, etc.) play a major role in outcomes.

Increasing antimicrobial resistance leaves few treatment options. Carbapenems are still the best treatment choice if the isolate is susceptible. Continuous or intermittent infusions correlate with therapeutic efficacy. Beta-lactamase inhibitors, particularly sulbactam, have intrinsic activity against acinetobacter strains. Monotherapy with sulbactam is not recommended for severe acinetobacter infection. Tigecycline, a new glycycline agent, has bacteriostatic activity against MDR-*A. baumannii*. High-level resistance to tigecycline has been detected among some MDR-*A. baumannii*. Furthermore, there is concern about whether adequate peak serum concentrations can be achieved. So tigecycline is best reserved for salvage therapy. Aminoglycoside agents, such as tobramycin and amikacin, are therapeutic options for infection with MDR-*A. baumannii* and

used in conjunction with another active antimicrobial agent. Clinicians have returned to the “old antibiotics” because of limited therapeutic options. Colistin acts by disturbing the bacterial cell membrane and it is bactericidal against *Acinetobacter* species. However colistin has poor lung and central nervous system distribution and there are concerns about its pharmacokinetics, pharmacodynamics and toxicodynamics. So it has to be reserved for salvage therapy. Aerosoli-

zed colistin may be an effective adjunctive intervention for the treatment of MDR-*A. baumannii* pneumonia.

For the treatment of *A. baumannii* infections, monotherapy is adequate if the patient does not have significant comorbidities. However, combination therapy can prevent the emergence of resistance.

The Control of *Acinetobacter* Infections in Hospital Settings

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Objective: *Acinetobacter baumannii* is an important cause of hospital infections in many hospitals, most often in critically ill patients admitted to intensive care units (ICU). The outbreaks caused by *A. baumannii* strains, that have acquired multiple mechanisms of antimicrobial drug resistance, make an increasing public health problem. The results of standard infection control interventions are often disappointing and new, more complex strategies are probably needed. We report here our experience in controlling *A. baumannii* outbreak occurred in our hospital, our never ending fight.

Methods: We conducted a retrospective study of 129 patients colonized/infected with *A. baumannii* in the ICU at University Clinical Hospital Mostar during the period between January 2009 and December 2010. The strains were identified by using current phenotypic methods, from the following samples: endotracheal tubus [(63) 48.8%], blood cultures [(24) 18.6%], bronchoaspirates [(16) 12.4%], wound swabs [(11) 8.5%], central venous catheters [(4) 3.1%], cerebro-spinal liquids [(2) 1.6%] and throat swabs [(9) 7%]. The antibiotic susceptibility testing was performed by using the disk-diffusion method against the antimicrobials: amoxicillin, amoxicillin/clavulanic acid, ampicillin/sulbactam, cefuroxime, ceftazidime, ceftriaxone, cefepime, gentamicin, amikacin, ciprofloxacin, levofloxacin, imipenem, meropenem and ertapenem, according to Clinical and Laboratory Standards Institute (CLSI) guidelines. In our institution, we have defined the multidrug resistant *A. baumannii* (MRAB), as acineto-

bacter isolates, that are resistant to two or more therapy-relevant antimicrobials.

Since 1998 a program for hospital infection control, mainly aimed to increase the hand-washing compliance, has been activated.

Results: From January 2009 to April 2009 we have observed an outbreak of MRAB. The first patient, with the multidrug resistant strain, was admitted in intensive care unit (ICU) from another hospital. During this period, 13 (68.5%) out of 19 isolated strains, were highly resistant (resistant to carbapenems and ampicillin/sulbactam). After the adoption of some specific precautions (i.e. contact cohort isolation of infected/colonized patients in a restricted area with specifically dedicated staff, hand washing priority and use of disposable gloves before and between patient contact for health care personnel and for all visitors), we have had the following results: from May 2009 to December 2010, 26 (23.6%) out of 110 isolated strains, were MRAB. The infection control program was further implemented and extended with a daily cleaning and periodic environmental disinfection.

Conclusion: MRAB can enter in the hospital by patients admitted from other hospitals and rapidly spreads across the wards representing a marker of the level of compliance with routine isolation precautions. Regular control requires good hand hygiene, barrier precautions and environmental decontamination. This study has showed that high standards of cleaning play an integral role in controlling outbreaks of MRAB in the intensive care unit setting.

Multiresistant Microflora in Nosocomial Infections

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Hospital infection (hospital, nosocomial)-current medical problem, important for the employs of any level of health. In the present review was dealt the latest information on nosocomial infection as natural consequence of a large array of permanent sources of pathogens in people coming to the hospital with unrecognized infectious diseases, close contact of patients and medical staff.

We presented herein statistics for Azerbaijan and abroad, analyzed the most frequently allocated nosocomial pathogens.

It was established that *Staphylococcus aureus* is the most common cause of mono-and mixed wound infection (article in Russian). It was determined that K_j value for common agents points to antagonism or associative interaction. During particular time periods of the study values of K_j significantly differed and defended from species. Specifically, for *Pseudomonas aeruginosa* the values of K_j were equal or exceeded 30% during several years.

According data of Georgian Cardiology Center (Tbilisi) nosocomial infections (Ni) still remain a serious problem in patients undergoing open heart surgery. The rate of Ni among 387 patient with congenital heart disease (CHD) was 16%. The most common infections were bloodst-

ream infections (7.75%) and respiratory tract infections (7%) respectively.

The rate of Ni was higher in patients under 1 year of age, after urgent surgery and urgent reoperation, long cardiopulmonary bypass, also in patients with prolonged mechanical ventilation, massive haemotransfusion, with open heart bone after surgery, reintubation. The evaluation of bacterial contamination of six hospital environment of Perinatal Center of Makhachkala as part of epidemiologic surveillance for Ni was established significant species diversity of opportunistic microorganisms: cultures of *Staphylococcus epidermidis* (46; 18.5%) and *Staphylococcus saprophyticus* (44; 17.7%) were significantly more frequently isolated from swabs from environment.

Ni's caused by multidrug resistant organism (MDRO) are an increasingly common healthcare-associated problem. In Surgery meticillin-resistant *S. aureus* (MRSA) is the most important of these bacteria, and the management of MRSA infections and the prevention of their nosocomial transmission are a major challenge in all over the world. Additionally, there is a high incidence of NI caused by beta-lactamase-producing gram-negative microorganisms in many regions of the world. These organisms are of clinical and epidemiological importance, since their mobile gene-

tic elements facilitate cross-infection (*Klebsiella pneumoniae*, *P. aeruginosa*, *Enterobacter* et al.) of gastrointestinal and urinary tract, respiratory system, bloodstream infection et al.

On the basis our data it was established, that the basic risk factors of *Candida*-and *Candida*-bacterial (*E. coli*, *S. epidermidis*, *P. aeruginosa*) associated nosocomial infection of urinary system are the prolonged and combined antibiotic therapy, the using of glucocorticosteroids and cytostatic drugs, and utilization during therapy by patients central venous and urine catheters, drainage tubes. It was also revealed, that urine from

patients with candidiasis of urinary system (US) stimulates the formation of *Candida*-biofilm on catheter materials, but the urine of healthy persons suppresses of their formation. The presence of glucose in urine of patients with nosocomial candidiasis of US also increased the risk of biofilm formation on catheters. It was also shown, that the one of factors, promoted the formation of associated *Candida*-staphylococcal biofilm is the significantly adhesion activity of *S. epidermidis* to intracellular matrix of *Candida albicans* biofilm.

Giant Viruses: Revisiting the Concept of Virus

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Many scientists attempted to elucidate the nature of viruses. Especially is unclear evolution of viruses. Are the viruses alive or not? Which domain of life do they belong to? What are relationships between viruses and cellular organisms? For many years, following concept of viruses was accepted: viruses are the smallest and simplest form of life, consisting of either DNA or RNA, protected by protein shell, and they are obligate intracellular parasite! Is it still so?

The discovery of giant Mimivirus (nucleocytoplasmic large DNA virus), its genome organization and replication cycle, challenged the established frontier between viruses and microorganisms. Even more, the recently discovered virus of Mimivirus (called Sputnik), has made the biggest boom in virology.

The Mimivirus size (> 400 nm), genome length (1.2 million bp) and large gene repertoire (> 900 protein coding genes) blur the old boundaries between viruses and microorganisms. Despite the many features making it unique in

the viral world, Mimivirus is nevertheless phylogenetically close to other large DNA viruses, such as phycodnaviruses and iridoviruses, and most likely share a common ancestry with nucleocytoplasmic large DNA viruses.

The discovery of giant viruses has stimulated a lot of discussions on the nature of viruses. There are two schools of thought. First, who defend the escape model, suggesting that Mimivirus is giant chimera, and second, who emphasize their uniqueness and ancient origin. Comparative genomics of nucleocytoplasmic large DNA viruses have produced a lot of data that have been interpreted according to the prejudices of the authors and thus failed until now to establish a consensus.

In this presentation, we discuss how the finding of a giant virus for the first time overlapping with the world of cellular organisms in terms of size and genome complexity might influence the way we look at microbial diversity, and force us to fundamentally revise our classification of domain.



Introduction to Parasitic Infections in Developing Countries

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Parasitic infections, particularly in developing countries, are still a major public health problem worldwide. According to the records, parasitic infections are the main reason for the tremendous mortality and morbidity and of over 300 million people affected at least half of the school-age children staying in developing countries. The poor and unhygienic conditions prevailing in many cities of the developing countries are unfortunately very ideal for the transmission of parasitic infections through the several ways such as; air, food, water, human waste or insect-vectors. The widespread neglected parasitic diseases include malaria, schistosomiasis, hook worm disease, leishmaniasis, giardiasis and amebiasis. Malaria, known to be the eighth leading contributor to global diseases burden measured in disability adjusted life years, poses a risk to almost 50% of the world's population over 100 countries.

In developing countries; it can obviously be suggested to supply following facilities for the control of parasitic diseases:

- Sufficient and proper public services, such as; water supply.
- Implementation of sanitation.
- Adequate and proficiency health services including laboratories which are capable of diagnosis and drug supplies for efficient treatment.
- Care, analysing and monitoring of obtained data from health services to state the distribution of parasitic diseases.
- Sustainance of vector control measures.
- Improvement of efficient vaccine for the parasitic disease

Percutaneous Treatment by Ormeci Method of Hydatid Cyst in the Liver

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Hydatic disease, caused by echinococcus granulosus, is still an important health problem leading obstructive jaundice, pain, compression of vessels and sudden death especially in endemic areas.

Aim of the study: We would like to present the results of long term follow up for the percutaneous treatment by Ormeci method of Hydatid Cyst in the liver.

Methods and patients: Three hundred and forty nine patients (female: n= 233, 66.8%, male: n= 116, 33.2% with hydatid cysts enrolled to study. Mean age was 45.71 ± 18.46 year. The location of the hydatid cysts in the liver were in the right lobe of the liver 82.5%, in the left lobe of liver 9.7%, bilateral 4%. Location was not available in 3.7% of the patients. According to Gharbi classification, Type I 9.7%, Type II 27.8%, Type III 4.9%,

68.8% of the patients (n= 240) were treated by ORMECI method. 8.3% of patients were treated by pure alcohol. 0.9 patients were treated only by polidocanol. 4% of patients were treated by abendazole.

Results: Mean diameter of the cyst was 81.61 ± 32.52 cm. before the treatment. Mean diameter of cysts was 69.08 ± 30.04 cm. Decreasing of diameter of the cyst was statistically significant ($p=0.001$). The duration of follow up was 34.52 ± 36.99 months. Daughter cysts reappeared in 6 patients. There were 3 anaphylactic reaction. They are alive after medical treatment. There was no death and fistulae in the treatment group.

Conclusion: The percutaneous treatment by ORMECI method of hydatid cysts is very safe, effective, easy to use and cheap. This method should be used for the treatment of hydatid disease...

Echinococcosis-Public Health Problem in Bosnia and Herzegovina

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Summary: Echinococcosis is parasitic disease of humans and animals. Small tapeworm is primary parasite in carnivore intestines. Disease occurs sporadically as endemic in rural and farmers regions in the world. Bosnia and Herzegovina (BiH) is endemic for cystic echinococcosis. After the war 1992/95 number of infected people is increasing.

Objective of this paper is to:

- Investigate frequency of echinococcosis in last 5 years
- Determine clinical forms and consequences of treated cases
- Indicate inadequate reporting of patients and inadequate prophylaxis of disease

Material and methods: Retrospective analysis of discharge letters of echinococcosis patients treated at Clinic for Infectious Diseases in period from 1.1.2005. to 31.12.2010., and analysis of Public health registers of patients with echinococcosis reported to Federal Institute of Public Health and Public Health Institute of Republic of Srpska (RS). Diagnosis was diagnosed with radiological methods and confir-

med serologically (ELISA or HI) and with pathohistological evaluation.

Results: Results show that in investigated period in BIH reported 189 patients, 31 in RS and 158 in FBIH. At Clinic for Infectious Diseases 47 patients with primary disease or postsurgical recidive was treated. In Kanton Sarajevo area 22 cases were reported. When we compare data from 2005-2010 with previous research from 2000-2004 data shows that further expansion of the disease or better reporting to Public Health officials.

For the research period at Clinic for Infectious Diseases among 47 patients, 43 of them were adult and 4 children. Average age is 42.4 (range 7-80). Echinococcosis of liver was found in 78% patients. We found three cases with skin echinococcosis, two of patients had lung echinococcosis, and also bone echinococcosis was found in two patients. Splenic cysts were found in one patient as well as renal cyst. Most of the patients (28) were treated with combined operative and medicament treatment with antihelminthic drug praziquantel. Ten patients were treated with combined surgically with antihelminthic therapy

consisted of albendazol and praziquantel and four patients were treated with PAIR method. There were no relapses of disease detected during 1-5 year follow up. Five patients are on prolonged albendazole therapy after surgical treatment (with bone echinococcosis, multiple muscular cysts, multiple lung cysts and postoperative liver cysts). Basic principle for prolonged treatment was clinical status controlled by imaging technique. Three patients were treated with PAIR method after combined surgical and medicament treatment after aseptic abscesses formed at residual pericysts.

Conclusions: Echinococcosis in Bosnia and Herzegovina is Public Health problem.

Reporting of disease is inadequate, real number and frequency of disease is unknown

Echinococcosis of liver was found in 76.6% cases.

Prevention of echinococcosis is poorly managed due to political problems.

Better cooperation of surgeon, pediatrician, internal medicine physician and radiologist with infectious disease specialist is needed.

Malaria: Current Views, an Ancient Problem

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Malaria is a protozoal disease caused by *Plasmodium* species. The parasites are transmitted to humans by female *Anopheles* mosquitoes. According to WHO data, there are approximately 300 million clinical cases of malaria and 1 million malaria related deaths annually in the endemic regions. The majority of the lethal infections are caused by *Plasmodium falciparum* infection in sub-Saharan Africa. Malaria is estimated to result in an economic loss of at least \$10 billion annually in Africa.

There are five species of parasites of the genus *Plasmodium* as a clinically significant pathogen in humans, which are *P. falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae* and *Plasmodium knowlesi*. The life cycle of the parasite species interchanges between the sexual cycle in the female *Anopheles* and the asexual cycle in the vertebrate host. Transmission occurs when the mosquito bites the human host and injects sporozoites into the bloodstream which then intrude on hepatocytes, where they develop into liver schizonts. Subsequently, hepatocytes rupture, thousands of merozoites are released and invade erythrocytes. This is the phase when all the clinical manifestations of the disease are encountered.

The disease is characterized by fever, chills, sweating, headache, malaise, and other systemic symptoms. In humans malaria related deaths are most commonly due to *P. falciparum*. Children aged six months to three years who live in endemic regions are particularly at risk.

Laboratory diagnosis of malaria should be confirmed by the identification of the parasites on thin and thick blood smear. Three times thick and thin smears should be obtained in a period of 12-24 hours. Alternative diagnostic methods may be used if the person does not have enough expertise in observing *Plasmodium* species in blood smears. The rapid diagnostic tests, new molecular techniques such as polymerase chain reaction (PCR) and nucleic acid sequence-based amplification (NASBA) are the current alternatives for diagnosis.

There is no single drug that can eradicate all forms of the *Plasmodium* species has been developed yet. Therefore, one or more different drugs are combined for malarial infection synergistically. *P. falciparum* shows widespread resistance against chloroquine. Resistance is rare in *P. vivax* infection. *P. ovale* and *P. malariae* still remain sensitive to chloroquine. Primaquine is required in the treatment of *P. ovale* and *P. vivax* infection in order to eliminate the liver hypnozoite forms.

Intravenous drugs are useable for the treatment of severe complicated malaria, admitting artesunate and quinidine gluconate. Monotherapy with artemisinin derivatives is not recommended, because of high rates of relapse. Artemether and lumefantrine tablets can be applied to treat acute uncomplicated malaria. Artesunate can be used intravenously. Various combinations such as atovaquone and proguanil HCL or quinine in combination with doxycycline or clindamycin are very effective. In patients from Southeast Asia the possibility of *P. knowlesi* infection should be kept in mind in the differential. This species frequently causes hyperparasitemia and more severe symptoms than non-falciparum mala-

ria. *P. knowlesi* infections should be treated in the same way as *P. falciparum*.

For the prevention of malaria, avoiding mosquito bites is important. Wearing long-sleeved clothing and using insect repellents are recommended. Using bed nets that are treated with permethrin is also useful. Chemoprophylaxis with antimalarials in patients travelling to endemic areas should be considered.

In conclusion, malaria is still one of the biggest health threats in the developing countries. Further researches are needed for the treatment and prevention.



Past and Future: Vaccination Against Protozoan Parasites

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Parasites plague billions of people and kill millions annually, and inflict debilitating injuries such as blindness, spontaneous abortion and anemia. Malaria kills more than a million people of all ages every year. About 3.3 billion people (half of the world's population) are at risk of malaria. WHO estimates the worldwide prevalence of leishmaniasis to be approximately 12 million cases, with annual mortality of about 60 000. The size of the population at risk is about 350 million. *Toxoplasma gondii* is an important medical parasite that infects approximately 30% of humans whereas amoebiasis is estimated to cause more than 100.000 deaths per year and reaching a prevalence of 50% of the general population. Trypanosomiasis remains also a significant public health issue and a major cause of morbidity and mortality in the world.

The recent advances in biotechnology have stimulated much research on the control of parasitic diseases through vaccination. There is as yet no effective vaccine for prevention of any parasitic disease. Attempts to develop vaccines against these pathogens have been hampered by the difficulty to cultivate them in vitro, the complexity of their multistage cycles and/or multicellular organization, added to their antigenic variability.

Several lines of evidence suggest that a prophylactic malaria vaccine for humans is feasible. Key obstacles to the development of a vaccine include the lack of predictive animal models, the lack of immune correlates of protection, in vitro immunoassays or functional assays, the antigenic diversity of the parasite, the stage-specificity of many induced immune responses and major economic hurdles. The traditional approach to develop malaria vaccines has been the targeting of the different stages of parasite development (pre-erythrocytic, asexual and sexual stages). A partially efficacious pre-erythrocytic vaccine would be expected to reduce the incidence of new blood stage infections. Asexual blood-stage (erythrocytic) vaccine would mostly serve as a disease-reduction vaccine in endemic countries by decreasing the exponential multiplication of merozoites. Vaccines targeting the sexual stage of the parasite or mosquito stages do not aim to prevent illness or infection in the vaccinated individual, but to prevent or decrease transmission of the parasite to new hosts.

At the time over 30 other malaria vaccine projects have reached the clinical evaluation stage. The most advanced and well-documented pre-erythrocytic vaccine candidate is derived

from the circumsporozoite protein (CSP) that is found at the surface of the sporozoite and of the infected hepatocyte. The pivotal multi-country Phase 3 registration trial of RTS,S/AS01 started in May 2009 and includes sites in Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique and Tanzania. The malaria vaccine technology road-map has a landmark goal of a vaccine with 50% efficacy against severe disease and death to be developed by 2015. RTS,S/AS01 may achieve this goal. The longer-term community goal is for a vaccine with 80% efficacy against clinical malaria and duration of protection of at least 4 years to be developed by 2025.

A first generation vaccine for leishmaniasis was prepared using whole killed parasites combined or not with BCG. Various subunit recombinant candidate vaccines also have been tested in mice and provided some degree of protection against leishmaniasis. These vaccines were based on: recombinant surface antigen gp63, a glycoprotein with protease activity, lipophosphoglycan, a surface glycoconjugate; a 46 kD promastigote antigen derived from *L. amazonensis*; or the *Leishmania*-activated C kinase (LACK), among others. Protection against *L. major* infection in mice was provided by DNA constructs encoding a number of *Leishmania* antigens, including gp63 and LACK. Recent evidence indicates that a 15

kD protein antigen derived from the salivary glands of the sandfly vector also could be protective in mice when given as a vaccine. Phase I trials of chimeric vaccine made of these three recombinant leishmanial antigens (LeIF, LmSTI-1 and TSA) in the form of a fusion protein combined with monophosphoryl lipid A in squalene oil as adjuvant in healthy volunteers in the USA and initial efficacy testing as a therapeutic vaccine in patients in Latin America suggest the safety and immunogenicity of the vaccine.

Actually *T. gondii* is medically important parasite that would be best controlled by vaccination. Current drugs are only effective against the tacyzoite stage of *T. gondii* and used reactivation during immunosuppression. Early vaccination attempts used killed *T. gondii*, lysates or crude extract. Viral delivery systems and eukaryotic expression vectors have been also used.

Evidence from a cohort of Bangladeshi children suggests that mucosal IgA directed against the major amoebic adherence molecule, a 170 kD lectin, correlates with resistance to reinfection with *E. histolytica*. Gerbils immunized with this lectin antigen were reported to show significant decrease of liver abscesses following parasite challenge, suggesting that a subunit vaccine might elicit protective immunity.



Oral Presentations



Genetic Diversity of Crimean-Congo Hemorrhagic Fever Viruses in Turkey

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Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne zoonosis widely common in Africa, Asia and Eastern Europe and Balkan Peninsula of the world. It has been also reported in Turkey with a remarkable high frequency. Reassortment and recombination events occurring in segmented RNA of CCHFV are associated with a worldwide genetic diversity. The aim of the present study was to investigate the genetic diversity and genetic relationship of CCHFV isolates derived from infected patients in a two-year period in several provinces of Turkey. Forty-eight patients' serum samples selected among the CCHFV RNA RT-PCR positive patients were subjected to sequence of partial S (48 samples) and M (14 samples) segments. The nucleotide alignments of the S and M segments showed the nucleic acid similarities among the tested viral RNA ranged from 95.7% to 100% and from 93.7% to 100%, respectively. Phylogenetic analysis of the both segments' sequences revealed that CCHFVs circulating in Turkey belonged to European lineage I and they were closely related to the viruses from Eastern European-Russian and Balkan Peninsula. M segment-based phylogenetic analysis was suggested that two of the CCHFVs (KYSR3159/09 and YZGT714/10) had additional genetic variation. The results of our present study indeed confirmed the close similarity and stability of CCHFVs circulating and causing infections in Turkey and the nucleotide variability of M-RNA segment resulting in frequent amino acid variations.

Key Words: Crimean-Congo hemorrhagic fever, genetic diversity, glycoprotein precursor, reassortment, recombination, Turkey



The H1N1 Influenza A Infection in 2009: University Clinical Hospital Mostar Experience

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OBJECTIVE: To describe the clinical course and outcome of hospitalized patients with H1N1 influenza A infection in 2009.

PATIENTS and METHODS: In this cross-sectional study, we reviewed the medical records of patients with H1N1 influenza A infection hospitalized at the University Clinical Hospital Mostar, from October 1st to December 31st, 2009.

RESULTS: Thirty patients with clinically and laboratory confirmed influenza A infection were hospitalized and treated at the University Clinical Hospital Mostar. Patient's average age was 38 years. In fifteen patients the H1N1 infection was virologically confirmed by real time PCR. Out of all H1N1 positive patients, eleven were males. Twelve of fifteen patients were middle aged, implicating that this age group was more affected by H1N1 infection as compared to seasonal influenza infection. All patients with H1N1 infection presented with symptoms like fever, cough, body aches and muscle pain, fatigue and headache. We did not see any difference between H1N1 positive and negative patients regarding co-morbidity. In addition, complications like pneumonia were equally distributed between H1N1- and seasonal influenza-infected patients. Among the H1N1 positive patients, thirteen of them developed acute lung inflammation or acute respiratory distress syndrome. However, most of infected patients required antibiotic treatment. Two patients required mechanical ventilation support, but despite of our intensive care they did not survive.

CONCLUSION: Hospitalized patients with H1N1 influenza infection are relatively young males, and a significant number of those patients required treatment at the University Clinical Hospital Mostar. Although azithromycin was mostly used, antibiotic therapy with moxifloxacin was more effective.

Key Words: Influenza A, H1N1, Mostar



The First Sandfly Fever Outbreak Reported in Kahramanmaras Province from East Mediterranean Region of Turkey

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Sandfly fever virus (SFV) is a RNA virus which is from Phleboviruses genus and *Bunyaviridae* family. SFV is transmitted to human by different species of sandflies and cause a self-limited febrile condition (three-day fever) known as sandfly fever. Four serotypes (Sicilian: SFSV, Naples: SFNV, Toscana: TOSV, and Cyprus; SFCV) that circulate in the Mediterranean area have been identified. After the first SFV outbreak in 2008 in Turkey, the virus activity and circulation has been observed every year in different areas.

Sandfly fever outbreak was seen with 9 “acute patients” in Kahramanmaras province (located in the East Mediterranean region of Turkey) during July-August 2010. There were history of fly bite and the clinical findings were fever, headache, myalgia, conjunctival hyperemia and gastrointestinal symptoms.

Of the patients, five were female and four were male. Laboratory findings were leucopenia, thrombocytopenia, elevated AST, elevated ALT, elevated CK, and elevated CRP. Serum samples were analyzed by using a commercial immunofluorescence test. The IgM positivity against to SFV was found in all cases (7 SFSV and 2 SFCV, serologically) and Sandfly IgG antibody was found in 6 patients. The two samples which were SFSV IgM positive, IgG negative were found to be positive for SFSV with real time PCR. All patients recovered with symptomatic treatment.

SFV is endemic in the Mediterranean basin and the data on SFV activity in Turkey is limited. This is the first report from East Mediterranean region of Turkey and provides knowledge for epidemiological, clinical and laboratory aspects of SFV infections.

Key Words: Kahramanmaras, Sandfly fever outbreak, phlebovirus, Turkey



Early Warning and Epidemic Intelligence in the Mediterranean Region and Balkans Countries

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EpiSouth was launched in December 2006, with the objective to improve communicable diseases control in Mediterranean countries. Among priorities, "Cross-Border Epidemic Intelligence", coordinated by the French Institute for Public Health Surveillance, aims to set up a framework for exchanging information on international and national health threats.

The different needs and expectations of the 27 EpiSouth countries on cross-border health risks management were evaluated through a questionnaire conducted in December 2007. As a result two major tools for early warning information exchanges have been elaborated: weekly Epidemiological Bulletin (eWEB) providing verified information on international health threats and a secured electronic platform allowing national alerts exchange.

All States declared the significance of early detection of emerging outbreaks in the international area that may affect their population. While all faced similar difficulties regarding control measures implementation, data exchange between countries, during large epidemics, has proven its usefulness: the efficacy of data sharing among EpiSouth countries was demonstrated in A (H1N1) pandemic and the recent West Nile fever outbreaks. The shared data of confirmed cases and deaths, national strategies, case management and immunization, gave a feed back on national level leading to updating their strategies.

The results illustrated a common understanding and expectation from epidemic intelligence throughout the area and underlined the need for formalised procedures. This high cohesion level from 27 Mediterranean countries that belong to three WHO regions, underlines the need to strengthen public health information sharing in the area, a challenge that EpiSouth PLUS project will fulfill in the coming years.

Key Words: Early warning, epidemic intelligence, infectious diseases surveillance, Mediterranean, Balkans, EpiSouth



EpiSouth Plus: A Project for the Control of Public Health Threats and Other Risks in the Mediterranean Region and South-East Europe

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BACKGROUND: The EpiSouth Network was established in 2006 by 9 EU Countries. It worked for the past four years in enhancing communicable diseases surveillance in the Mediterranean region and includes 27 countries (9 EU and 17 non-EU, plus one candidate country). It is therefore the biggest inter-country collaborative effort of this kind in the region.

METHODS: A new phase of activities started in October 2010 and foresees a shift to a wider approach. Building on knowledge of gaps and needs identified during the first phase, the EpiSouth-Plus Project aims at contributing to the control of public health threats in the Mediterranean region and South-East Europe. EpiSouth-Plus is co-financed by EU DG-SANCO/EAHC, EuropeAid and the national participating Institutions together with the Italian MOH and ECDC.

EXPECTED RESULTS: Seven work packages co-lead by EU and non-EU countries ensure the following:

1. To facilitate common threat detection by establishing a Regional Laboratories Network.
2. To enhance Mediterranean Early Warning (EW) functions through interoperability with other EW platforms and especially the European EWRS as forecasted by the current EU legislation.
3. To promote common procedures in interoperable Generic Preparedness and Risk Management.
4. To facilitate IHR implementation through assessments on national procedural and legislative aspects.

CONCLUSIONS: The project promotes knowledge, resource and information sharing, regional cohesion and stability. Strategic documents, providing a novel basis for regional policies in health threats assessment and control, will be produced. The reinforcement of relations of trust is an objective and an instrument in the scope of Project's implementation.

Key Words: Network, early warning, IHR-2005, generic preparedness plan, laboratory, health threats



Comparative Inhibitory Effect of *Camiella sinensis* (Green Tea) Aqueous Non-Fermented, Fermented and Semi Fermented Extracts Against *Helicobacter pylori*

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BACKGROUND: The growing problem of antibiotic resistance by the organism in Pakistan thus demands the search for novel compounds, especially from natural sources as in this study.

METHODS: In this study, a total of 400 biopsies were collected from the patients of gastro-duodenal pathology who were referred for endoscopy in a public sector hospital in Karachi, Pakistan. All these biopsies were processed for detection of *H. pylori* by two rapid Helicourease - indigenously developed rapid urease detection kits, culture and polymerase chain reaction (PCR). The 5% aqueous extract of fermented, semi fermented and non-fermented green tea was prepared and their antibacterial potential was explored against 35 clinical isolates of *H. pylori* agar well diffusion technique. The minimum inhibitory concentration (MIC) of the most susceptible tea products were also carried out by micro-dilution method for the sake of comparison.

RESULTS: A total of 120, clinical *H. pylori* isolates were successfully cultured and identified by rapid and molecular methods. Most of the screened *H. pylori* isolates were resistant to more than one of the antibiotics like metronidazole and clarithromycin. The most significant activity was obtained in non-fermented green tea with an average zone of inhibition along with MIC was around 32 mm (MIC 120-150 µg/mL), semi fermented product showed 28 mm (MIC 140-200 µg/mL) showed and fermented one showed 32 mm (MIC 120-200 µg/mL).

Key Words: *Camiella sinensis*, *H. pylori*, inhibitory effect



Doxycycline-Rifampin Versus Doxycycline-Rifampin-Gentamicin in Treatment of Human Brucellosis

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In a retrospective study carried out at the Clinic for Infectious Diseases in Skopje, the therapeutic efficacy and safety of two anti-microbial combinations in 92 patients with brucellosis has been compared. Included patients were classified in two groups according to the therapeutic protocol. Patients from the first group, a total of 55, received a combination with doxycycline and rifampin with duration of 45 days. The other group included 37 patients treated with doxycycline, and rifampin during 45 days, and gentamicin for the first 7-10 days. The final processing of the outcome after at least 6 months post-therapy, showed 7 (12.7%) relapses in the first group and 3 (8.1%) relapses in the second group ($p=0.485$). No serious adverse effects were registered. The results suggest that both anti-microbial combinations are equally efficient and secure in treatment of acute forms of human brucellosis. However, prospective, randomized trials that comprise larger number of patients and longer follow-up are needed for definite conclusions.

Key Words: Brucellosis, therapy, gentamicin, doxycycline, rifampin



Neurobrucellosis: Hearing Loss and Accompanying Disturbance of Seven Cases

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BACKGROUND: Brucellosis is an endemic zoonosis in Southern Turkey. Neurobrucellosis occurs in 5-10% of cases of brucellosis and affects the central (CNS) or peripheral nervous system (PNS). These manifestations are diffuse encephalopathy/meningoencephalitis, inflammatory peripheral neuritis/radiculitis, inflammatory demyelinating syndromes.

METHODS: A retrospective analysis of 7 cases of neurobrucellosis was carried out.

RESULTS: Headache, fever, hearing loss, walking disability were the predominant symptoms, while dysarthria, ataxia walking, bilateral sensorineural hearing loss, and increased deep tendon reflexes were the most frequent findings. The major complications in our patients were cranial nerve involvement, polyneuropathy/radiculopathy, depression, paraplegia, stroke and hearing loss. The most commonly-used antibiotics were combinations of rifampin, doxycycline, and trimethoprim-sulfamethoxazole.

CONCLUSION: Neurobrucellosis should be considered in accompanying fever the unexplained neurological symptoms such as hearing loss, cognitive dysfunction, young transient ischemic attacks, paraparesis, and psychiatric symptoms, especially in those who live in endemic areas.

Key Words: Neurobrucellosis, hearing loss, walking insability, neurological symptoms



A Nationwide Study on Cervical Lymphadenitis in Turkey: Tuberculosis or Tularemia?

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Cervical tuberculous lymphadenitis (CTL) and oropharyngeal tularemia (OT) cases have significantly increased in recent years in Turkey. Till 2010, the number of extrathoracic tuberculous lymphadenitis cases in all tuberculosis cases have raised from 1622 to 2036 between the years of 2005 and 2009 with the ratio of 7.9% and 11.7%, respectively. Similarly, OT cases have also increased in this period. In this study, we aimed to investigate tularemia seroprevalence in patients diagnosed with CTL.

Patients diagnosed between the years of 2008 and 2011 with CTL in tuberculosis control dispensaries in all provinces of Turkey were informed about this study. The sera obtained from volunteers were tested for tularemia by micro agglutination. Antibodies to *Brucella* were also investigated with tube agglutination test for cross reactions in the sera which was seropositive for tularemia.

Sera of patients from 67 of 81 cities were tested. Antibodies to *Francisella tularensis* in 79 of 1170 sera were positive with a titer of 1:80 or higher. Considering this titers, OT was accounted for 6.75% of all CTL cases. When the presence of antibody in any titer was considered, the ratio became 8.20% (96/1170). Antibody titers to *Brucella* were $\geq 1:160$ and 1:40 in two cases as demonstrated by tularemia micro agglutination test with the titers of $\geq 1:2560$ and 1:20, respectively.

First time with this study, tularemia serology was found positive in a significant portion of CTL cases. It was concluded that tularemia serology should be investigated in patients suspected with CTL.

Key Words: Tuberculous lymphadenitis, oropharyngeal tularemia, micro agglutination test for tularemia



Odontogenic *Streptococcus bovis* Meningitis in a Patient with Waldenstrom Macroglobulinemia and Splenectomy

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INTRODUCTION: *Streptococcus bovis* is a member of oral and gastrointestinal flora. It may cause endocarditis or septicemia especially in patients with colorectal malignancy where lower gastrointestinal tract (GIT) is a portal of entry, but it is a rare cause of central nervous system (CNS) infection. Here, we report a case of *S. bovis* meningitis developing 10 days after dental procedure.

CASE: A 59-year old female patient presented with fever, sore throat, nausea, and vomiting. In her medical history, she had Waldenstrom macroglobulinemia and splenectomy. Although she had no signs of meningeal irritation, a lumbar puncture revealed increased pressure, turbid appearance of cerebrospinal fluid (CSF), with 1040 leukocytes/mm³ (90% neutrophils), elevated CSF protein (248 mg/dL) and decreased glucose (15 mg/dL) concentration (serum glucose: 98 mg/dL). Gram-positive cocci and abundant leukocytes were seen on CSF smear. *S. bovis* was isolated in CSF culture and it was susceptible to penicillin. Fourteen days of ceftriaxone 2 x 2 g IV treatment was given for acute bacterial meningitis. Her gastrointestinal exploration excluded malignancy.

DISCUSSION: *S. bovis* is a rare cause of central nervous system infection. In this patient, possible hematogenous dissemination after dental extraction had resulted in odontogenic *S. bovis* meningitis, which has been reported very rarely in the literature. Waldenstrom macroglobulinemia, splenectomy and extraction of infected tooth could be predisposing conditions for development of meningitis in our patient. Colonoscopy should be performed in such cases to rule out colorectal malignancy. Antimicrobial prophylaxis before/during dental procedure could prevent development of serious infections in such patients.

Key Words: *Streptococcus bovis*, meningitis, odontogenic, dental extraction, Waldenstrom macroglobulinemia, splenectomy, antimicrobial prophylaxis



An Audit of Dengue Fever Cases in the Year 2010 at Civil Hospital Karachi-Pakistan

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BACKGROUND: Dengue virus is endemic in Pakistan, and occurs throughout the year, but with often with peaks in certain seasons.

METHODS: Patients suffering from high grade fever visiting medical and paediatrics outpatient departments as well as indoor patients of Civil Hospital, Karachi, Pakistan, in the year 2010 (from January to December) were included in this study. Patients were initially screened for platelet count and test for Dengue fever. Blood was collected aseptically and CBC (Platelet count) was done on Sysmex Haematology autoanalyser and test for Dengue antibodies IgM and IgG was done by Rapid Immunochromatography and ELISA technique.

RESULTS: Total 2321 patients were screened for Dengue fever, out of these 585 were reported positive for Dengue fever i-e 25.2 %384 were males while 201 were females. Dengue antibodies IgM and IgG (ICT) was done on 1118 samples, 585 were positive for IgM alone or both for IgM and IgG. i-e 26.39% Dengue antibodies IgM and IgG (ELISA) was done on 260 samples 87 were positive for IgM (33%) and 28 were positive for IgG alone (10.77%). However, Dengue antigen was done on 943 samples, 175 samples were reported positive for Dengue antigen (18.5%). The result analysis indicated that the age group most affected was 20-40 years. Male /female ratio was found 2:1. Besides this, 90% patients had low platelet count i-e less than 100.000/cumm, 10% had normal or near normal platelet count most of them showed decrease in platelet count later on.

Key Words: Dengue fever, civil hospital, audit



The Impact of Teleconference Establishment to Reduce Infection Rate in Intensive Care Unit of a Tertiary Level Hospital

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INTRODUCTION: Hospital acquired infections (HAIs) have a higher incidence in intensive care units (ICUs) and responsible for higher hospitalization and mortality rates. HAIs increase costs of patient care. There are statements on architecture and indoor decoration of ICU. But there is not well defined documents about relations of patients' visitors. We aimed to compare two different periods of HAIs attack rate before and after teleconference system (TCS) establishment.

MATERIALS and METHODS: TCS includes two high definition cameras and TVs which is settled in visitor's and patient care area to blockade physical contact. We compared overall HAIs, UTI, pneumonia, bloodstream infection rates, for six months period, before and after TCS establishment. Descriptive statistic methods were used.

RESULTS: Results summarized in Table 1 and 2.

CONCLUSION: In conclusion, we found that overall HAIs attack rate and bloodstream infection incidence decreased significantly but there was no significant decrease in urinary tract infections and pneumonia.

Key Words: Teleconference, intensive care unit, hospital acquired infections

Table 1. Infection attack rate in ICU six months period before and after establishment of teleconference system

	HAI		Total
	Yes (n)	No (n)	
Before	78	234	312
After	48	233	281
Total	126	467	593

Table 2. Types of HAI in ICU

	UTIs	Pneumonia	Bloodstream infections
Before	11	33	32
After	7	24	16
p value	0.4	0.4	0.04



Characteristics and Results of Fungal Bloodstream Infections in Intensive Care Unit

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INTRODUCTION: Fungal pathogens commonly affect patients in the intensive care unit (ICU) and carry a high risk for mortality. We aimed to evaluate candida bloodstream infections in intensive care unit for clinical and laboratory characteristics and mortality risks.

METHOD: This study was carried out January 2008 to December 2010 in an intensive care unit. Underlying factors for fungemia, risk factors for mortality and distribution of isolated yeast species were investigated retrospectively.

RESULTS: Twenty-eighth fungemic patients were included to the study. Of the patients 18 (64.3%) were male and mean age was 52 (+2.8). A total of 30 yeasts were isolated from blood cultures samples of 28 patients. *Candida albicans* (43%) was the most frequently isolated species. All isolates were sensitive to fluconazole. The mortality rate was 53.6%. In the deceased group albumin was lower, CRP and APACHE II scores were significantly higher than living group. There was no significant relation between mortality and total antibiotic days, used antibiotic groups before fungemia. Sepsis and multiorgan failure was seen 93% and 69% respectively. Mean antifungal treatment initiation time after receiving blood culture was 68.7 and 46 hours for died and living groups respectively. In alive group the mean blood culture negativity was obtained within 5 days.

CONCLUSION: Bloodstream fungal infections in ICUs are associated with severe sepsis and high mortality rates. Delay in treatment cause high mortality. Empirical antifungal therapy according to the surveillance data should be given to high risk patients for candida infection without delay.

Key Words: Fungal bloodstream infection ICU

Impact of Antibiotic Restriction Policies on Consumption of Restricted Antibiotics Between 2005 and 2010 in Turkey

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BACKGROUND: There has been many laws and arrangements of the government that affects antibiotic consumption in Turkey. Since 2003, some of the antibiotics can be prescribed only by the approval of infectious diseases specialist. The aim of this study is to present the consumption of some broad spectrum antibiotics between 2005 and 2010.

METHODS: The data about whole country is obtained from Turkey IMS Pharmacies. The Anatomical Therapeutical Chemical (ATC) coded data is converted to standardized data as defined daily dose (DDD)/1000 inhabitant days. For conversion to DDD, WHO web site is used and the number of inhabitants in Turkey is obtained from web site of Turkey Statistics Foundation.

RESULTS: The data about the consumption rates of broad spectrum antibiotics used to treat severe infections between 2005 and 2010 in Turkey is shown in the Table 1.

CONCLUSIONS: According to the results of the study;

1. Despite these restrictions, antibiotic utilization has increased in Turkey.
2. The consumption of cephalosporins, carbapenems and antifungal drugs has increased significantly.
3. Antibiotic consumption may be influenced by the suggestions of guidelines (for example cefepime).
4. Drug consumptions decreases when there is no support of pharmaceutical industry.
5. Constitution of standard national treatment protocols, updates of these protocols, and extended postgraduate training programs will contribute to the rational antibiotic consumption.

Key Words: Antibiotic, restriction

Table 1. Consumption of some broad spectrum antibiotics used to treat severe infections between 2005 and 2010 in Turkey (DDD/1000 inhabitant days)

Antibiotic	2005	2006	2007	2008	2009	2010
Imipenem	0.0033	0.0050	0.0062	0,0098	0.0094	0.0116
Meropenem	0.0025	0.0034	0.0049	0,0048	0.0063	0.0076
Ertapenem	0.0000	0.0000	0.0000	0,0004	0.0010	0.0013
Doripenem	0.0000	0.0000	0.0000	0,0000	0.0000	0.0010
Ceftazidime	0.0013	0.0007	0.0009	0,0009	0.0008	0.0013
Cefepime	0.0029	0.0022	0.0005	0,0017	0.0009	0.0011
Cefoperazone-sulbactam	0.0019	0.0022	0.0037	0,0054	0.0053	0.0057
Piperacillin-tazobactam	0.0004	0.0004	0.0007	0.0011	0.0010	0.0014
Tigecycline	0.0000	0.0000	0.0000	0.0000	0.0127	0.0267
Vancomycin	0.0022	0.0032	0.0037	0.0041	0.0036	0.0048
Teicoplanin	0.0090	0.0114	0.0125	0.0166	0.0107	0.0093
Linezolid	0.0000	0.0002	0.0006	0.0016	0.0017	0.0024
Fluconazole	0.0168	0.0178	0.0244	0.0325	0.0374	0.0426
Amphotericin B	0.0009	0.0012	0.0013	0.0018	0.0009	0.0016
Voriconazole	0.0000	0.0003	0.0007	0.0020	0.0032	0.0029
Itraconazole	0.0001	0.0001	0.0003	0.0003	0.0004	0.0012
Caspofungin	0.0001	0.0001	0.0002	0.0004	0.0007	0.0009
Total	0.2508	0.2641	0.2908	0.3717	0.3856	0.4838



High Dose Colistin for the Treatment of Multidrug Resistant *Acinetobacter baumannii* Ventilator-Associated Pneumonia: Does It Increase Nephrotoxicity?

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OBJECTIVE: To assess the safety and efficacy of colistin (COL) in the treatment of multidrug resistant *Acinetobacter baumannii* ventilator associated pneumonia (VAP).

METHODS: Adult critically ill patients, received COL for multidrug resistant *A. baumannii* VAP, was evaluated retrospectively.

RESULTS: A total of 20 patients were evaluated [9 patients with high dose COL (600 mg), 7 patients with standard dose (300 mg), 4 patients with low dose according to creatine clearance]. Aerosolized COL was used in 14 patients concomitantly with IV COL. Clinical response rate at the fifth day was 29%, 0% and 33% with standard, low and high dose respectively. However, clinical response rate at 14th day declined to 14%, 0% and 0% with standard, low and high dose respectively. Microbiological response rate was 71%, 75% and 56% at the fifth day and 71%, 50% and 44% at the 14th day, with standard, low and high dose respectively. Clinical response rate at the fifth and 14th day was 21% and 0% with aerosolized COL, whereas it was 33% and 17% without aerosolized COL. Microbiological response rate at the fifth and 14th day was 64% with aerosolized COL, whereas it was 67% and 33% without aerosolized COL. Nephrotoxicity rate was 56% in high dose, while it was 29% in standard and 50% in low-dose.

CONCLUSION: High dose seems not safe and effective in multidrug resistant *A. baumannii* VAP. COL had high nephrotoxicity rates in patients with renal insufficiency, even if the dose adjusted according to serum creatine clearance. Aerosolized COL did not have additional effect on clinical response.

Key Words: Colistin, *Acinetobacter baumannii*, ventilator associated pneumonia, nephrotoxicity, response rate.

Diabetic Foot Infections: Comparing of Deep Soft Tissue and Bone Tissue Biopsy Samples Cultivation

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INTRODUCTION: Factor related treatment reduce the risk of high grade diabetic foot amputation, treatment period and cost effect is significant. For this purpose patients with diabetic foot infection deep tissue and bone biopsy culture have examined.

METHODS: In this medical research Sisli Etfal Training and Research Hospital Wound Committee's 30 patients with high grade diabetic foot submitted to amputation or debridement. For microbiological analysis deep tissue and/or bone biopsy samples had taken. We performed aerobic and anaerobic methods to cultivation. Deep tissue and bone biopsy culture results were compared.

RESULTS: Deep tissue and bone biopsy samples taken from 20 of the 30 patients and solely deep tissue samples taken from 10 patients. 27 of the 30 (90%) samples culture resulted positive. 19 of the 27 cultivations resulted as single microorganism, eight were polymicrobial. Two different microorganisms were isolated from these polymicrobial cultivations.

16 of the 20 (80%) patients' bone biopsy samples had positive cultivation results. Single microorganism isolated from 9 of 16 samples, seven were polymicrobial. Two different microorganism were isolated from six of these polymicrobial cultivations.

CONCLUSIONS: In this study 5 (25%) patients' deep tissue and bone biopsy culture results showed difference. It reveals that using microbiologic studies of deep tissue samples solely, resulted treatment failure in 25% of the patients. Simultaneously performed microbiologic study both deep tissue and bone biopsy culture will improve the success of the treatment.

Key Words: Diabetic foot, deep tissue culture, bone biopsy culture.

Figure 1

Microbiologic results of deep tissue biopsy samples

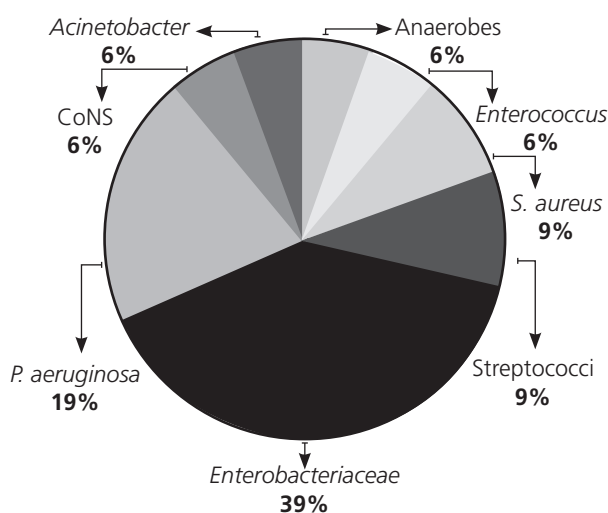
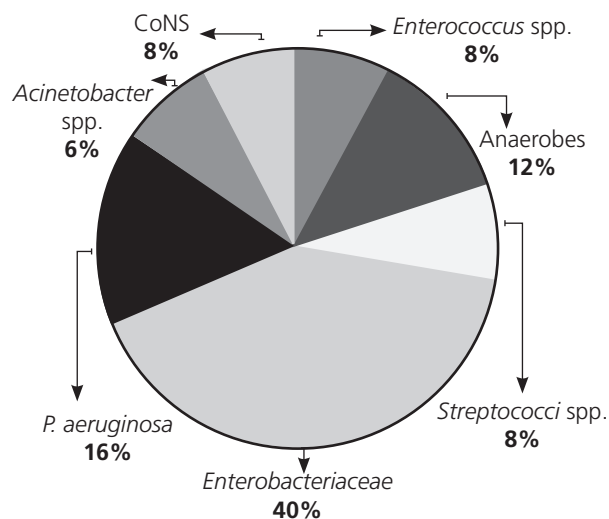


Figure 2

Microbiologic results of bone tissue biopsy samples





Stevens-Johnson Syndrome and Infectious Diseases

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INTRODUCTION: Stevens-Johnson syndrome (SJS) is a serious, life-threatening inflammatory disease that involves the skin and mucous membranes, but also affects other vital organs. The annual incidence of SJS is estimated to be between 1 and 2 cases per million inhabitants. SJS is an immune-complex-mediated hypersensitivity disorder that is most often elicited by drugs and infections and because of that is not rare among infectious diseases.

OBJECTIVE: To examine etiologic and clinical features of Stevens-Johnson syndrome and to identify possible correlates of clinical disease severity related to etiologic findings.

PATIENTS and METHODS: In this study, we retrospectively analysed laboratory and clinical features three patients with brucellosis and SJS, two females and male, and compared with those of the two young boys with *Mycoplasma pneumoniae* induced SJS.

RESULTS: Antibiotics were the possibility causative factors of SJS among all brucella patients (mean age 57.3 years). The mean interval between drug administration and SJS was 20 days (range, 19-22 days). All of them had skin, mucous membranes and ocular involvement. Patients with mycoplasma infections had "atypical SJS" presented with severe mucositis, without typical skin disorders. Corticosteroids were the most common systemic therapy. One patient had chronic ocular sequelae with consecutive blindness.

CONCLUSION: Our clinical findings corroborate those in previous reports that the more severe form SJS is usually caused by reactions to medications, rather than infections.

Key Words: Stevens-Johnson syndrome, infections



Evaluation of Fast-ELISA versus Standard ELISA to Diagnose Human Fasciolosis

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The present study was conducted to evaluate and compare a fast-ELISA (F-ELISA) method versus standard-ELISA (S-ELISA) to diagnose human fasciolosis. Serum samples were obtained from 35 individuals infected with fasciolosis, 27 infected with other parasitoses and 22 from healthy people. The samples were examined with S-ELISA (30 min incubation periods) and F-ELISA (10 min incubation periods) for total antibody response against fasciolosis. The optimum conditions for S-ELISA and F-ELISA were respectively as follows: antigen 10 and 5 µg/mL, sera 1:500 dilution for both, peroxidase-conjugated goat anti-human IgG diluted 1:7000 and 1:10.000. Data were analyzed using SPSS version 11.0. Cut-off value for S-ELISA and F-ELISA was determined as 0.56 and 0.42, respectively. The sensitivity, specificity; positive and negative predictive values were detected as 97.2%, 100%, 94.6%, and 95.6% for both tests. Cut-off values, sensitivity, specificity and other important parameters of two evaluated tests, witness that F-ELISA method can be exploited with no sensed difference.

Key Words: Fasciola, Enzyme-Linked immunosorbent assay, diagnosis, validity

Serum Paraoxonase and Arylesterase Activities and Oxidant Status in Patients with Brucellosis

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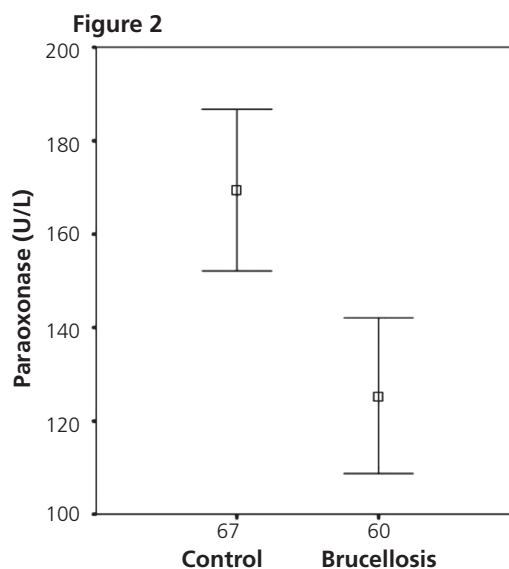
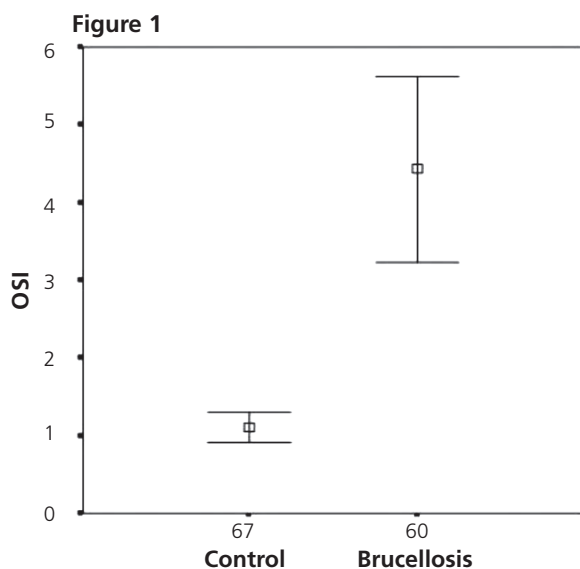
OBJECTIVES: The aim of this study was to investigate the effect of brucellosis infection on paraoxonase-1 (PON1) activity and oxidative status in patients with brucellosis.

METHODS: Sixty patients with brucellosis (47 acute, 13 subacute) and 67 healthy controls were included in the study. Serum PON1 and arylesterase activities, total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI), total free sulfhydryl (-SH), and lipid hydroperoxide (LOOH) groups were determined. In addition, HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG) were measured.

RESULTS: Serum PON1 and arylesterase activities, total -SH group levels and TAC were significantly lower in brucellosis patients than controls ($p < 0.001$). TOS, OSI and LOOH levels were significantly higher in brucellosis patients than controls ($p < 0.001$). There were no significant differences between serum LDL-C, TG and TC levels of patients compared to controls ($p > 0.05$).

CONCLUSIONS: Patients with brucellosis are exposed to potent oxidative stress and they have decreased PON1 activity. These predispositional factors might play a role in the pathogenesis for atherosclerosis in patients with brucellosis.

Key Words: Brucellosis, PON1 activity, oxidative status, atherosclerosis



PON1 activity, oxidant and antioxidant parameters in patients and the control group

Parameters	Patients (n= 60) Mean \pm SD	Control (n= 67) Mean \pm SD	p value
Paraoxonase (U/L)	117.85 \pm 43.42	162.57 \pm 40.06	< 0.001
Arylesterase (kU/L)	125.39 \pm 64.42	169.49 \pm 72.2	< 0.001
-SH (mmol/L)	0.32 \pm 0.01	0.54 \pm 0.06	< 0.001
TAC (mmol Trolox Equiv./L)	1.27 \pm 0.21	1.38 \pm 0.16	< 0.001
LOOH (μ mol H ₂ O ₂ equiv./L)	33.72 \pm 42.82	6.93 \pm 3.62	< 0.001
TOS (μ mol H ₂ O ₂ Equiv./L)	50.32 \pm 45.81	15.05 \pm 10.42	< 0.001
OSI (arbitrary unit)	4.41 \pm 4.60	1.10 \pm 0.79	< 0.001

The First Imported Chikungunya Case in Turkey

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Chikungunya virus is an arthropod-borne alphavirus that causes an acute febrile illness named Chikungunya fever. Chikungunya fever outbreaks have been reported from India since 2006. Here we report the first Chikungunya case imported from India, New-Delhi to Turkey.

In December 2010, 55 years old female Turkish government employee living in urban area of New Delhi for the last 3 years, had sudden onset fever up to 38.4°C for 2 days. Itching rash and arthralgia were also occurred. Symptomatic treatment was given in New Delhi. She returned to Turkey and because of continuing arthralgia was admitted to Infectious Diseases Unit of Hacettepe University Hospital in the 26th day of her complaints. She had hepatomegaly in physical examination. Serum of the patient was anti-Hanta and anti-Dengue virus serotypes 1-4 IgM and IgG negative, but positive for anti-Chikungunya virus IgM and IgG with IFA (Euroimmun) technique and sample was found to be negative with the real-time RT-PCR for Chikungunya in Refik Saydam National Public Health Agency Virology laboratory.

This is the first laboratory confirmed imported Chikungunya case in Turkey. There are mosquitoes of *Aedes* species that can transmit this virus in Turkey. This case report will be an alert for the clinicians in Turkey while evaluating the patients with fever, arthralgia and rash to consider the diagnosis of Chikungunya fever also.

Key Words: Chikungunya, first imported case, Turkey

Positive IFA for anti-Chikungunya IgM

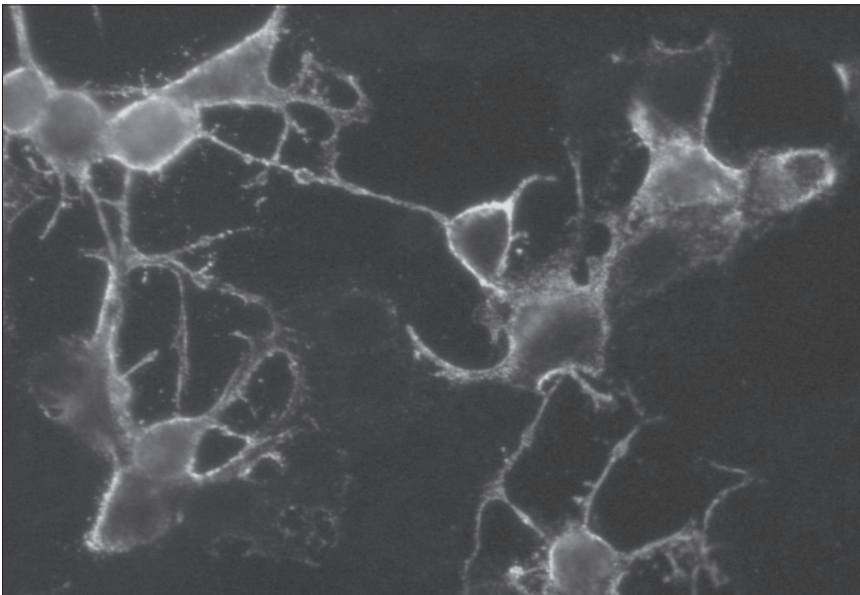


Figure 1. Image under the x40 objective.



Acute Viral Hepatitis A Infection In HBsAg (+) Hosts: 24 Case Reports

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There is insufficient information on clinical course of acute HAV infection and its effect on HBV serology in a HBsAg (+) host.

Between 2004-2010, we evaluated 24 cases of acute HAV infection with a concomitant positivity for HBsAg. We performed a 6 months follow-up for each patient. Mean age was 22 (18-27) years. Male/female ratio was 16/8. All cases were icteric and had acute symptoms by their administration. At the same time, mean SGOT and SGPT values were over 900 IU/L, total bilirubin levels were over 10 mg/dL and direct bilirubin predominance was observed. Alkaline phosphatase values ranged between 250-350 IU/L, GGT values between 50-100 IU/L in this study group. Albumin and globulin values were within normal limits. We observed hepatitis markers as anti-HAVIgM (+), HBsAg (+), anti-HBcIgM (-), anti-HBctotal (+), HBeAg (-), anti-HBe (+), anti-HCV (-), anti-Delta (-) for each case. In clinical follow-ups, all patients showed clinical and biochemical improvement. In 2 cases (male 18 years old, female 20 years old) at the end of our follow-up in 6 months, we recorded anti-HAVIgM (-), HBsAg (-) and anti-HBs (+). Both these cases developed seroconversion, in a total rate of 8.3%. Remainder of the cases were anti-HAVIgM (-) and HBsAg (+).

In conclusion; spontaneous loss of HBsAg is reported to be at 2.3-2.9% per year among non-replicative HBV carriers. Our result on this subject was observed in a rate of 8.3% in our 24 patients. A second antigenic stimulation due to an acute HAV infection may contribute the possibility of developing a seroconversion in patients who do not display seroconversion and do not have insufficient immune response against HBsAg. This topic requires more medical investigations and study reports by larger series in order to achieve a more elaborate and precise result.

Key Words: Acute viral hepatitis A, HBsAg, seroconversion



Ethiology of Bacterial Meningitis in Children in Tuzla Canton

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BACKGROUND: Bacterial meningitis is a serious infectious disease of children. It is an important cause of morbidity and mortality.

AIM: To identify the most common causes of bacterial meningitis in children and to represent its epidemiology in Tuzla Canton.

PATIENTS and METHODS: This is a retrospective study which included 140 children, aged 1 month to 14 years, treated at the Clinic for Infectious Diseases Tuzla, in the period 1999-2009, who had clinical and laboratory parameters of bacterial meningitis.

RESULTS: In Tuzla Canton in 10 year period were registered 140 cases of bacterial meningitis in children aged 1 month to 14 years. Prevalence was 1.53/1000. The average age of patients with bacterial meningitis was 3.6 ± 3.8 years. Male to female ratio was 1.3/1. April, May and November were the months with the most reported cases of bacterial meningitis ($p=0.02$). Most affected were children 1-12 months of age, and least children 11-14 years of age ($p<0.001$). The most common pathogens of bacterial meningitis were *Haemophilus influenzae* (13.6%), *Neisseria meningitidis* (8.6%) and *Streptococcus pneumoniae* (5.7%) ($p<0.001$). *Haemophilus influenzae* was the most common cause of bacterial meningitis in the age groups 1-12 and 13-24 months ($p=0.034$). Mortality was 2.14%.

CONCLUSION: Bacterial meningitis is present in Tuzla Canton, and three major pathogens are *Haemophilus influenzae*, *Neisseria meningitidis* and *Streptococcus pneumoniae*. The most affected were children 1-12 months of age. Most cases of meningitis occurred in spring.

Key Words: Bacterial meningitis, children, causes, epidemiology, Tuzla Canton



Posters

Antimicrobials

001-050



Tigecycline Use in a Tertiary Care Hospital

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OBJECTIVES: Multidrug and extremely-resistant (MDR, XDR) gram-negative bacteria associated nosocomial infections are becoming one of the major problems in the hospital settings. A glycylycline antibiotic, tigecycline, was shown to be effective against many MDR bacteria. The aim of this study is to determine the parameters of the use of tigecycline in our hospital since 2008; the indications, and adherence to the guidelines.

METHODS: Documents regarding tigecycline use between May-2008 and December-2010 were investigated from archives of the hospital pharmacy and the infection control committee of the hospital.

RESULTS: Totally 119 tigecycline use were determined from 111 in patients (56 female). Mean age was 62 (17-93). Total hospitalization days were 7751. 80.7% of the use was from ICUs. 40.2% of total was from anesthesiology and reanimation-ICU followed by neurology-ICU (17.6%), neurosurgery-ICU (11.8%), internal medicine-ICU (6.7%) and surgery-ICU (2.5%). The main bacteria that tigecycline was used against of was *Acinetobacter baumannii* (84.9%) followed by *Klebsiella pneumoniae* (3.4%), *Escherichia coli* (2.5%) and *Enterobacter* spp. (1.7%). 5.9% of total was used empirically. Clinical indications were as follows: ventilatory associated pneumonia (VAP) (37%), blood stream infections (16%), soft tissue infections (16%), urinary tract infections (13.4%), surgical site infections (5.9%) and intra-abdominal infections (2.5%). In 9 (7.6%) patients there were multiple site infections and 2 (1.7%) patients had meningitis.

CONCLUSION: Although tigecycline is not approved for VAP, the main use was VAP in our experience because of the high percentage of XDR *A. baumannii* in our ICUs. The adherence to the guidelines was found to be low.

Key Words: Tigecycline, *Acinetobacter* spp., ICUs



Critical Evaluation of Antibiotic Use in a University Hospital

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BACKGROUND and AIM: Antibiotics are being used unnecessary and incorrect characteristic because of different reasons. We evaluated antibiotic practice at Dicle University Hospital in an observational approach. The aims were assessment of quality of antibiotic use and determine the factors associated with correct usage of antibiotics inpatients.

METHODS: Antibiotic use of inpatients was assessed with a surveillance study in 2006. Using a standardized data collection form, the patients' data (clinic, epidemiology, laboratory and antibiotic use) was collected. At the same time, antibiotic use was assessed by an infectious disease specialist. Possible influencing factors on antibiotic use were examined.

RESULTS: In the surveillance study, 1350 inpatients were evaluated that 461 of them (34.1%) were using antibiotic for treatment and 187 (13.9%) for prophylaxis. Antibiotic indication was found 355 of 461 patients (77.0%) in the treatment group. In 243 patients, antibiotic usage was completely accurate. In the prophylaxis group, 81.5% of the patients had indication for antibiotic prophylaxis and in 54.4% of the cases correct antibiotic was chosen. In 86.5% of the patients, the duration of the antibiotic prophylaxis was longer than necessary (mean 6.5 days).

In the multivariate analyses, application for emerging surgical reason ($p=0.016$), clinical manifestation of infection at the beginning ($p=0.000$), critical situation at the beginning ($p=0.000$), and presence of leukocyte counting ($p=0.001$) were found significant positive factors for correct indication decision. Application with a diagnosis other than infection was found a significant negative factor for 'correct indication' decision. In multivariate analyses, clinical manifestation of infection at the beginning ($p=0.000$), presence of leukocyte counting ($p=0.000$), critical situation ($p=0.000$) and making decision by infectious disease specialist were found significant positive factors for completely accurate antibiotic use. Application with a diagnosis other than infection was found a significant negative factor for completely accurate antibiotic use ($p=0.001$).

CONCLUSION: The quality of antibiotic use could be improved with better clinical and laboratory diagnose and consultation with infectious diseases specialists.

Key Words: Antibiotic use, quality, evaluation, associated factors



Antibiotic Susceptibilities of *Staphylococcus aureus* Isolated from Blood Cultures Between 2008-2010

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OBJECTIVE: *Staphylococcus aureus* is one of the most common etiologic agent of bloodstream infection acquired in hospital or in the community. The purpose of this study was to determine the antibiotic resistance rates of *S. aureus* strains isolated from bloodstream infection.

METHODS: A total of 103 isolates, each from a unique patient, were received from Gulhane Medical Military Academy from January 2008 to December 2010. Identification and antibiotic susceptibility testing were performed by automated Phoenix system (BD).

RESULTS: A total 103 *S. aureus* strains were identified from different patients. Of the 103 *S. aureus* strains, 37 (35.9%) were MRSA (methicillin resistant *S. aureus*) and 66 (64.1%) were MSSA (methicillin susceptible *S. aureus*). The resistance rates of MRSA to other antibiotics were as follows: 78.3% resistant to erythromycin, 56.7% to clindamycin, 29.7% to trimethoprim-sulfamethoxazole, 91.8% to ciprofloxacin, 77.7% to levofloxacin, 77.7% to moxifloxacin, 100% to penicillin G, 83.7% to rifampin, and 83.3% to tetracycline. No MRSA strain resistant to vancomycin, teicoplanin and linezolid, was recorded in this study. The resistance rates of MSSA to other antibiotics were as follows: 16.6% resistant to erythromycin, 4.5% to clindamycin, 4.5% to trimethoprim-sulfamethoxazole 7.5% to ciprofloxacin, 6% to levofloxacin, 3% to moxifloxacin, 93.9% to penicillin G, 1.5% to rifampin and 7.5% to tetracycline. No MSSA strain resistant to vancomycin, teicoplanin and linezolid was recorded in this study.

CONCLUSION: Antimicrobial susceptibility profile of susceptible and resistant strains of *S. aureus* strains should be provided for better management of BSI and determine their probable causes.

Key Words: Bloodstream infections



Antimicrobial Resistance of *Acinetobacter baumannii* strains Isolated from Clinical Specimens in Tekirdag, Turkey

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In this study, antimicrobial susceptibility patterns of *Acinetobacter baumannii* strains isolated from clinical specimens sent from various clinics to the microbiology laboratory were investigated. Antimicrobial susceptibility testing was carried out by the Kirby-Bauer disk diffusion method and the results were assessed according to the guidelines of the Clinical and Laboratory Standards Institute.

A total of 218 strains of *A. baumannii* were isolated in Tekirdag State Hospital in 2010. *A. baumannii* strains were isolated from, blood (39.4%), endotracheal aspirate (45.8%), wound (8.7%), urine (3.6%), sputum (1.3%), throat (0.4%) and ear (0.4%) samples. The resistance rates of the isolates were; 98.6%, 97.2%, 65.6%, 90.8%, 84.9%, 97.2%, 97.2%, 98.2%, 99.1%, 97.7%, 81.6%, 86.7%, 96.3%, 92.7%, 93.6% to ampicillin, cefotaxime, gentamycine, cefazoline, tetracycline, trimethoprim-sulfamethoxazole, amoxicillin-clavulonic acid, ceftazidime, sefuroxime, ceftoxime, imipenem, meropenem, ciprofloxacin, cefepime, piperacillin-tazobactam, respectively.

Our results demonstrated, the antimicrobial resistance of *A. baumannii* is an emerging problem in Tekirdag. The importance of continuous monitoring of antimicrobial susceptibility and strict adherence to infection prevention guidelines are emphasized.

Key Words: *Acinetobacter baumannii*, antimicrobial resistance



Evaluation of In Vitro Activity of Fosfomycin Against Urinary *Escherichia coli* Isolates

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Fosfomycin is an antimicrobial commonly used in uncomplicated urinary tract infections. The aim of this study was to evaluate the in vitro activity of fosfomycin against *Escherichia coli* strains isolated from urine specimens.

Data were retrieved from two hospitals in Tekirdag, Turkey. We retrospectively examined the susceptibility results of *E. coli* strains to fosfomycin, collected over one year (January 2010-March 2011). Susceptibility of the isolates was determined by disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) criteria.

A total of 561 *E. coli* strains were examined. Out of the isolates 34 (6.06%) were resistant to fosfomycin. Resistance was highest amongst isolates (25 of 34; 73.52%) taken from outpatients and sent from the urology clinics (16 of 34; 47.05%).

According to data obtained from this study, fosfomycin seems to exhibit good levels of in vitro activity against urinary *E. coli* isolates in our region. Further evaluation of its potential clinical effectiveness is needed to justify these in-vitro antimicrobial susceptibility results.

Key Words: *Escherichia coli*, fosfomycin, antimicrobial susceptibility



To the Question of Etiology and Treatment of Suppurative Inflammatory Ear, Nose, Throat (ENT) Diseases of Children

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AIM: Suppurative inflammatory diseases at child's hospitals demand special emphasis from the direction of the study their etiological factors and effective treatment with the regarding formed polyresistant strains of microbes to antibiotics.

OBJECTIVES: There were examined 324 children in age from 2-15 years old with different pyogenic inflammatory processes of nose, ear and throat.

RESULTS: In 232 (72%) patients pathogens have been cultured and identified, and in 28% of all cases microorganisms were not identified. The most particular pathogen remained *Staphylococcus* spp., however in 36% of all cases *S. aureus* was isolated, in 33% of all cases *S. epidermidis* was identified. Group A streptococci was isolated in 5 patients. There were detected gram-negative microflora in 33 sick children, from them the most frequent culture was *P. aeruginosa* (10%), from 7 patients isolated *Proteus* spp., 2 - *E. coli*, 1 was *Enterobacter* spp. Microbial association took place in 10% of all cases.

The research of antibiotic susceptibility of *S. aureus* showed highest susceptibility to rifampin 92.5%, ofloxacin-87.2%, ciprofloxacin-71.8% and lowest was shown to penicillin-3.9%, ampicillin-5.5%, tetracycline-44%.

P. aeruginosa was highly susceptible to azlocillin-79.1%, amikacin-76.7% and low susceptibility to gentamicin-44.3%.

CONCLUSION: Thereby in the structure of suppurative inflammatory diseases in the age of child is remained *S. aureus* as etiologic factor, at the second position is gram-negative flora such as *P. aeruginosa*, *E. coli*, *Proteus* spp. The role of microbial association has increased, which make more difficult treatment of this contingent of patients.

Key Words: Suppurative inflammatory diseases, antibiotic resistance



Bacteriological Investigations in Practise of Hospital Infections

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The success of struggle with nosocomial infections depends on the quality diagnosis and adequate use of the treatment. In 25% of all nosocomial diseases are surgical infections of soft tissues.

Mutagenic action of antimicrobials promotes to appear intrahospital nosocomial strains of microorganisms.

During comprehensive clinical, bacteriological research patients with pyogenic inflammatory processes of soft tissues isolated 930 strains of different types of microbes. From that number of isolates the frequent pathogens are *S. aureus*-245 (26.3%), *S. epidermidis*-183 (19.6%), *E. coli*-217 (23.3%), *P. aeruginosa*-197 (21.1%), *Klebsiella* spp.-88 (9.4). In patients with suppurative processes of closed cavity oftenly found monocultures and bacterial associations are seen rarely.

The previous our investigations on evaluations of antibiotic resistance showed tendency of increasing resistance of *S. aureus* to ampicillin, azitromycin, erythromycin, tetracycline, most of isolates of *S. aureus* in 59.4% were characterized as polyresistant.

The frequency of microbial resistance isolated from hospitalized patients to cephalosporin unambiguously. The studied strains of staphylococci were often resistant to action of cefasolin (49.3%), cefotaxim (53.2%), and cefepim (45.8%).

Amongst strains of *E. coli* frequency of resistant to cephalosporin of I-III-IV generation was vary in the level 34.8% on account of cefamandol and cefalexin to which *E. coli* was susceptible in 100% of all cases.

As is obvious from the foregoing our obtained results can't be considered exhaustive and not absolute arraignment shows the antibiotic resistance condition of microbes. Probably only obligatory monitoring of antibiotic resistance microorganisms with summarizing the correct data.

Key Words: Nosocomial infections, pyogenic infectious diseases, antibiotic resistance



The Increasing Resistance in Nosocomial *Acinetobacter* Isolates in Turkey: 1993-2009

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INTRODUCTION: *Acinetobacter* spp. has become the most important nosocomial pathogen in Turkey because of their resistance rates. Increasing resistance of carbapenem is an area of great concern. The aim of this study was to evaluate the resistance rates of nosocomial *Acinetobacter* isolates according to the years 1993 to 2009.

METHODS: Pubmed and Turkish Medline were searched for terms of "*Acinetobacter* and resistance and Turkey". The literatures which evaluate the resistance of nosocomial *Acinetobacter* spp. according to Clinical Laboratory Standarts Institutes criteria for antibiotic susceptibility since 1993 to 2010 from Turkey were included in the study.

RESULTS: Eighty-two manuscripts were included in the study. It is found that resistance rate of *Acinetobacter* isolates rose from 33.1% in 1993-1997 to 79.7% in 2008-2009 for imipenem and rose from 8.8% in 1993-1997 to 82.3% in 2008-2009 for meropenem. The lowest level of resistance was observed against cefoperazone/sulbactam (59.9%), netilmicin (24.9%), colistin (2.4%) and tigecycline (0.8%).

CONCLUSION: Carbapenem resistance is getting a serious problem in Turkey as in the world. Colistin and tigecycline seem most effective agents for empirical usage if there is a clinical suspicion of multidrug resistant *Acinetobacter* infection.

Key Words: *Acinetobacter*, nosocomial, resistance, Turkey



Colistin and Tigecyclin Sensitivity Among Carbapenem and Cefoperazon-Sulbactam Resistant from Our Intensive Care Unit *Acinetobacter* Strains

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INTRODUCTION: Acinetobacteries are mainly from arise from intensive care units (*Acinetobacter* species is mainly arising from intensive care units). They are factors (It is causes of bacteriemia, sepsis, nosocomial pneumonia and urinary tractus infections. Acinetobacters developed rapidly resistance to carbapenems, cefoperazon sulbactam and other wide-spectrum antibiotics in years. Thus, acinetobacter induced (infections caused by acinetobacter) may respond to limited treatment strategies (options).

OBJECTIVE: In this present study, we elaborated (examined) carbapenem and cefoperazon/sulbactam resistant acinetobacter strains for tigecyclin and colistin sensitivity.

METHOD: Between the dates of January 2009 to January 2011, we included carbapenem and cefoperazon/sulbactam resistant acinetobacter strains to our study as infectious factors. These strains were defined (identified) by mini-API semi-automatic bacterial identification system (bioMerriex). Antibiotic sensitivities (susceptibly) were determined by Kirby-Bauer disc diffusion method through CLSI advisories.

RESULTS: In total, we detected 30 cases. In these cases we investigated tigecyclin and colistin sensitivity. 15 strains were from tracheal aspirate (50%), 5 strains were from phlegm (16.6%), 5 strains were from blood culture (16.6%) and the last 5 strains were from catheters (16.6%). All isolates were sensitive to tigecyclin and colistin sensitivity (100%).

CONCLUSION: *Acinetobacter* strains which were derived from our intensive care unit did not exhibit (show) in-vitro tigecyclin and colistin resistance. The infections caused by these carbapenem and cefoperazon/sulbactam resistant acinetobacter strains require treatment with colistin and tigecyclin in appropriate indications.

Key Words: *Acinetobacter*, colistin, tigecyclin



Imipenem, Meropenem and Ertapenem Sensitivity in ESBL Positive *Escherichia coli* and *Klebsiella pneumoniae*

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INTRODUCTION: ESBL producing gram-negative bacteria are reported to be in an enhancing rate among population and nosocomial origin infections. Infections involving these bacteria present a limited treatment options. Medication of choice in these group is carbapenems.

OBJECTIVE: Between the dates of January 2009 to January 2011, we summarized our data which was derived from clinical examples producing ESBL *E. coli* (n= 15) and *Klebsiella pneumoniae* (n= 20). We aimed to measure sensitivities for imipenem, meropenem and ertapenem by disc diffusion method.

METHOD: Thirty five strains were included to the study. ESBL productivity in these strains were studied by BD Phoenix (Sparks, USA), automatized identification and antibiotic sensitivity detection system and combined disc (cefotaxime/clavulonic acid, ceftazidim/ceftazidim clavulonic acid). Imipenem, meropenem and ertapenem sensitivities determined by disc diffusion method through CLSI advisories.

RESULTS: Fifteen samples were tracheal aspirates (42.85%), 10 samples were from phlegm (28.57%) and the last 10 samples were from blood culture. Five samples (14.28%) were resistant to meropenem, 2 samples (0.57%) were resistant to imipenem. All samples were sensitive to ertapenem (100%).

CONCLUSION: ESBL producing gram-negative bacteria present resistance to several antibiotics. For carbapenem group antibiotics, we did not observe any resistance at the initial time period. Afterwards, in recent years, we coincide resistance to carbapenem. In our study, there were no ertapenem resistant sample. On the other hand, there was a limited resistance to imipenem and meropenem. As a conclusion, we state that these group of antibiotics can be applied for these infections.

Key Words: ESBL, imipenem, meropenem, ertapenem



A Case of Ertapenem-Induced Visual Hallucination

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INTRODUCTION: Ertapenem is a long-acting, 1 beta-methyl parenteral Group 1 carbapenem antibiotic that has a broad antibacterial spectrum and once-a-day dosing. It is active against both gram-positive and gram-negative bacteria. In this study, we report a case of ertapenem-induced visual hallucination in a patient with diabetic foot infection.

CASE: A 64-year-old man was admitted to our hospital with nausea, vomiting, fever, an injury of his left leg. History revealed that he had type 2 diabetes mellitus and chronic renal failure. First toe of his left foot had been surgically amputated a month ago. On physical examination he had a stinking necrotic tissue 5 x 5 cm in diameter, beside the first toe of his left foot. The ulcerated tissues were partially debrided. Specimens showed ESBL positive *E. coli* growth. Sefaperazon-sulbactam therapy was started. On the 8th day of the treatment the patient encountered a gastrointestinal bleeding. Sefaperazon-sulbactam therapy was replaced with ertapenem 0.5 g once a day IV. On the 6th day of ertapenem therapy, the patient had cognitive changes, disarthria and spontaneous movements of the extremities. Meningeal irritation and lateralizing signs were absent on neurological examination. Cranial MR and EEG were normal. Neurology consultant concluded that spontaneous movements of the extremities were related with visual hallucinations. Ertapenem was exchanged with piperacilin-tazobactam and metronidazol. The patient's neurological signs were diminished next day.

CONCLUSION: We report a case of who had visual hallucinations associated with ertapenem use. To our knowledge, this is the first report of ertapenem-induced visual hallucination.

Key Words: Ertapenem, visual hallucination, diabetic foot infection



Convulsion Induced by Imipenem in a Patient with Acute Pancreatitis

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INTRODUCTION: Imipenem, member of the carbapenem class of beta-lactam antibiotics, is among the most broadly active antibiotic available for systemic use in humans. Similar to other beta-lactam antibacterials, carbapenems have a neurotoxic potential that seems to be higher than that of the penicillins and cephalosporins. In this study, we report a case of imipenem-induced convulsion in a patient with acute pancreatitis.

CASE: A 82 years-old man admitted to the emergency room with abdominal pain, and fever. On admission, his serum chemistry results revealed the following values: amylase, 491 IU/L; and lipase, 247 IU/L. Ultrasonographic examination showed that pancreas has a hypochoic and edematous appearance and the border of pancreas was unclear because of peripancreatic adipose tissue inflammation. Dynamic contrast-enhanced computed tomography scan of the pancreas revealed an increase in size of the pancreas and heterogeneous pancreatic parenchyma. Patient was hospitalized with diagnosis of acute pancreatitis and operated. *E. coli* and *Citrobacter* spp. were isolated on blood agar culture of intraabdominal material. The patient was treated with imipenem/cilastatin, but developed convulsion with tonic-clonic myospasms at 15th day of therapy. The treatment of imipenem was exchanged with meropenem because of imipenem's close relation with convulsions. The patient's convulsions were diminished next day. Electroencephalography was normal. We could not find any other possible etiologic cause of convulsion by physical examination and laboratory evaluation.

CONCLUSION: Seizures have occurred in patients treated with imipenem/cilastatin. Clinicians should be aware of the convulsion that may be induced by imipenem in a patient with acute pancreatitis.

Key Words: Imipenem, pancreatitis, convulsion



Detection of Caspofungin Susceptibility in Bloodstream Isolates of *Candida* by Broth Microdilution Method and E-test

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OBJECTIVE: Caspofungin is the first echinocandin antifungal licensed globally. When compared with the natural compound, an improved antifungal activity against *Candida* and more favourable pharmacokinetic properties were obtained by modulation of the chemical structure of pneumocandin B0. The aim of this study is to evaluate the susceptibilities of bloodstream isolates *Candida* to caspofungin.

MATERIALS and METHODS: A total 167 *Candida* isolates were collected in the clinical routine. The yeasts were identified by standard taxonomic procedures and the identification was confirmed by the API 20C AUX. In vitro susceptibilities to caspofungin were determined using the broth microdilution method described in the CLSI M27-A3 document and E-test. MICs were noted after 24 and 48 hours of incubation. The most frequently isolated species was *Candida albicans*. Among the non-albicans species *Candida tropicalis* was the most prevalent, followed by *Candida parapsilosis*, *Candida glabrata*, *Candida kefyr* and *Candida krusei*.

RESULTS: The 24 h MIC values of caspofungin obtained from broth microdilution method and E-test have been found as follows: *C. albicans* (0.03-1/0.03-1 µg/mL), *C. tropicalis* (0.03-1/0.03-1 µg/mL), *C. parapsilosis* (0.03-1 / 0.02-1 µg/mL), *C. glabrata* (0.06-1/0.06-0.75 µg/mL), *C. kefyr* (0.03-0.125/0.03-0.125 µg/mL) and *C. krusei* (0.125-1 / 0.016-1 µg/mL) (Table 1).

DISCUSSION: As a result, in vitro data obtained in this study suggest that caspofungin showed good in vitro activity against bloodstream *Candida* isolates and the caspofungin E-test MICs correlated well with the microdilution MICs.

Key Words: Caspofungin, *Candida* spp., E-test

Table 1. Minimal inhibitory concentration (MIC) data of caspofungin for *Candida* spp.

<i>Candida</i> spp.	MIC range (µg/mL)			MIC range (µg/mL)		
	Microdilution method			E-test method		
	MIC range	MIC ₅₀	MIC ₉₀	MIC range	MIC ₅₀	MIC ₉₀
<i>C. albicans</i> (n= 40)	0.03-1	0.06	0.25	0.03-1	0.5	0.5
<i>C. tropicalis</i> (n= 35)	0.03-1	0.125	0.5	0.03-1	0.125	0.5
<i>C. parapsilosis</i> (n= 30)	0.03-1	0.125	0.5	0.02-1	0.125	0.125
<i>C. glabrata</i> (n= 25)	0.06-1	0.25	0.5	0.06-0.75	0.125	0.5
<i>C. kefyr</i> (n= 20)	0.03-0.125	0.06	0.125	0.03-0.125	0.125	0.125
<i>C. krusei</i> (n= 17)	0.125-1	0.25	0.5	0.016-1	0.125	0.5



Antimicrobial Investigation of Some N-[β -(3,5-di and 1,3,5-trisubstituted pyrazol-4-yl) alkyl]amides

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In order to overcome rapid development of drug resistance, new agents should preferably consist of chemical characteristics that clearly differ from those of existing agents.

In this study, antimicrobial activity of some N-[β -(3,5-di and 1,3,5-trisubstituted pyrazol-4-yl)alkyl]amides (a total of 11 compounds) were tested using microbroth dilution method against seven of bacteria *Streptococcus faecalis* NRRL B-14617, *Salmonella typhimurium* NRRL B-4420, *Staphylococcus aureus* NRRL B-767, *Escherichia coli* ATCC 25922, *Bacillus subtilis* NRRL 744, *Listeria monocytogenes* ATCC and a yeast (*Candida glabrata*) in vitro. Chloramphenicol and ketakonazole were used as control drugs.

MICs were recorded as the minimum concentration of a compound that inhibits the growth of tested microorganisms. All of the compounds tested were illustrated significant antibacterial and antifungal activity when compared with reference drugs. The MIC values are generally within the range of 62.5-250 μ g/mL against all evaluated strains. *C. glabrata* was the most susceptible organisms against many of the compounds tested (K6, K7, K8, 3, 5, 12) when compared with ketaconazole. Therefore these compounds may be evaluated in synthesis of antifungals.

Key Words: Antimicrobial resistance, MIC, antibacterial and antifungal activity



Distribution and Antimicrobial Susceptibility Profiles of the *Enterobacteriaceae* Isolated from Urinary Tract Infections at Policlinic Patients at a Tertiary Care Hospital in Canakkale, Turkey

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Between January 2009 and January 2011, 3733 urine samples were sent to our laboratory from policlinics. Significant growth was detected at 584 of these, and 254 *Enterobacteriaceae* spp. were included in this study.

Samples were inoculated to 5% sheep blood and EMB agar. Identification and antibiograms were performed by Vitek 2 Compact system. Antibiograms were evaluated according to CLSI criteria.

Isolates were detected from 199 female and 55 male patients with average age 45.7 (min 1, max 93). The distribution of 254 isolates were; 213 *E. coli* (83.8%), 21 *K. pneumoniae* (8.2%), 6 *K. oxytoca* (2.3%), 4 *Enterobacter* spp. (1.5%), 3 *Citrobacter* spp. (1.1%), 3 *Proteus* spp. (1.1%), 2 *Morganella morganii* (0.7%), 2 *Serratia* spp. (0.7%).

The overall susceptibility rates were; for ampicillin 33%, for amoxicillin/clavulanat 63.3%, for cefepime 82.6%, for ceftriaxone 81.1%, for ceftiofloxacin 88.5%, for cefuroxime 70.4%, for gentamicin 79.1%, for amikacin 77.1%, for ciprofloxacin 67.7%, for co-trimoxazole 53.9%, for fosfomycin 94.4%, for nitrofurantoin 83.8%. No carbapenem resistance was detected. At the study, 51 isolates (20%) were found ESBL (+). While 43 (97.7%) of the 44 ESBL (+) *E. coli* strains were found susceptible against fosfomycin, 40 (90.9%) were susceptible against nitrofurantoin and 33 (75%) were susceptible against ciprofloxacin.

It is important to know regional antibiotic susceptibility profile to start empiric medical treatment of urinary tract infections at policlinic patients. According to the results from this study, fosfomycin can be thought as an alternative agent for treatment of the policlinic patients.

Key Words: Antimicrobials, urinary tract infections



Correlation with Minimal Inhibitory Concentration Values and Mortality in *Staphylococcus aureus* Bacteremic Patients

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Treatment failure due to growing methicillin-resistance in *Staphylococcus aureus* strains (MRSA) and increasing vancomycin MIC values in MRSA maintains its importance. It is crucial to determine the MIC values of glycopeptides and other new antibiotics (tigecycline, linezolid, daptomycin) for the success of antimicrobial treatment. Here, we report the MIC values of 103 *S. aureus* strains isolated from blood cultures and describe the correlation between methicillin resistance and mortality.

Of the 103 strains, 26 were MRSA (25%), and 77 were MSSA (75%). No resistance was observed for vancomycin, teicoplanin, linezolid or daptomycin. Six MRSA and 3 MSSA strains were detected as tigecycline-resistant. MIC₉₀ value for vancomycin was determined as 1.5 µg/mL. In 39 MSSA and 21 MRSA strains, the MIC values of vancomycin were detected over 1 µg/mL. The rate of MRSA strains with an MIC value over 1 µg/mL was significantly higher than the rate of MSSA isolates with an MIC value over 1 mg/mL ($p < 0.007$). Mortality rate was 10% ($n = 8$) in MSSA bacteremias, while the mortality rate in MRSA was 38% ($n = 10$) indicating a significant correlation between methicillin resistance and mortality ($p < 0.001$). Methicillin resistance is associated with higher MIC values, increased need for intensive care, prolonged hospital stay and increased mortality rate. Therefore, when using glycopeptides in the treatment of MRSA infections, the MIC values should be closely monitored. Regular monitoring of resistance patterns is important to determine empirical treatment.

Key Words: *Staphylococcus aureus*, bacteremia, methicillin resistance, vancomycin, minimal inhibitory concentration, mortality

Table 1. Correlation between methicillin resistance and mortality

	Survive	Death	Total	p value
MSSA	69 (89.6%)	8 (10.3%)	77	
MRSA	16 (61.5%)	10 (38%)	26	< 0.001
Total	85 (82.5%)	18 (17.4%)	103	



A Case of Multidrug Resistant *Acinetobacter baumannii* Infection Treated with Tigecycline

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INTRODUCTION: Acinobacters are commonly identified agents especially in the VAP (ventilator associated pneumoniae). Resistance to many antibiotics, including carbapenems leads to significant problems. In this paper we reported a case of multidrug resistant *Acinetobacter baumannii* VAP in the ICU treated with tigecycline.

CASE REPORT: A 54 year-old-male patient with exacerbation of COPD and hypercapnic respiratory failure had been followed in the chest diseases department and ceftriaxone 2 x 1 g IV was commenced empirically. The patient was intubated due to general condition deterioration and loss of consciousness and was admitted to ICU. On the 15th day of treatment deep tracheal aspirate cultures were taken due to fever, increase in the tracheal secretions and pneumonic infiltration on chest radiography. Colistin-resistant *Acinetobacter* spp. was isolated in the culture. Tigecycline 2 x 50 mg and amikacin 1 g IV was commenced. Lung infection completely resolved after 15 days.

DISCUSSION: Resistant *Acinetobacter* infections have been seen especially in intensive care units with increasing frequency in recent years. Despite the adverse side effects, polymyxin derivatives have been introduced again for the treatment of these infections, recently and they have been the only option for the most of time. However resistant strains of *Acinetobacter* to these antibiotics have emerged and have been reported with increasing frequency. Tigecycline may be an option in these strains. Therefore, determining tigecycline sensitivity of the bacteria in intensive care units is very important. We believe that colistin resistant, tigecycline sensitive *Acinetobacter* infections could be treated successfully with this antibiotic as in this case.

Key Words: *Acinetobacter*, tigecycline



The Comparison of High-Level Aminoglycoside Resistance Between Vancomycin Resistant and Sensitive Enterococci Isolated from Clinical Samples

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This study aimed at investigation of high-level aminoglycoside resistance in vancomycin-resistant enterococci (VRE) and vancomycin-sensitive enterococci, and comparison of their resistance rates. It was investigated in 200 strains, 100 VRE and 100 vancomycin-sensitive enterococci, isolated in our laboratory in materials sent from clinics of Haydarpasa Numune Training and Research Hospital. API 20 Strep (bioMerieux) kit was used for identification of isolated strains. Brain-heart infusion (BHI) agar containing 6 µg/mL vancomycin was used to detect vancomycin resistance and MIC value of vancomycin was determined by E-test method. BHI agar containing 500 µg/mL gentamycin was used for detection of high-level gentamycin resistance (HLGR), whereas BHI agar containing 2000 µg/mL high-level streptomycin resistance (HLSR) was used for streptomycin resistance. All VRE strains were determined to be *E. faecium*. 53%, 42%, 3%, and 2% of vancomycin-sensitive enterococci strains were detected to be *E. faecalis*, *E. faecium*, *E. durans*, *E. avium*, respectively. High-level vancomycin resistance (MIC > 256 µg/mL) was determined in all VRE strains. VRE strains showed HLGR by 83% and HLSR by 89%, while their co-existence is present in 78% of isolates. In vancomycin-sensitive strains, 42% showed HLGR and 48% showed HLSR, while HLGR-HLSR co-existence was detected in 36% of strains. It was determined that incidence of HLGR, HLSR, and HLSR-HLGR co-existence was statistically significantly higher in VRE strains compared to vancomycin-sensitive enterococci ($p < 0.005$).

Key Words: Vancomycin-resistant enterococci, high-level gentamycin resistance, high-level streptomycin resistance



Investigation of Antimicrobial Activity of Tigecycline Against Extended Spectrum Beta-Lactamase Positive *Escherichia coli* and *Klebsiella* spp. Strains

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Tigecycline is the first commercially available member of the glycolcyclines, a new class of antimicrobial agents. The drug is active against many gram-positive and gram-negative organisms, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci and extended-spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae*. Carbapenems have been used to treat infections caused by ESBL producing *E. coli* and *Klebsiella* species. However, treatment options of infections caused by carbapenemase producing gram-negative bacteria are limited.

The aim of this study was to investigate the in-vitro activity of tigecycline against ESBL producing *E. coli* and *Klebsiella* strains isolated from various clinical specimens. The study was carried out at Microbiology Laboratory of Konya Training and Research Hospital in January-June 2010.

The isolates included 50 *E. coli* and 30 *Klebsiella* spp. Thirty five (43%) of them were isolated from clinical samples belongs to outpatients and 45 (57%) inpatients. The identification of microorganisms and susceptibility testing were performed using the Phoenix automated system (BD, USA).

The isolates were recovered from the following sources: urine (69%), wounds (16%), blood (6%) and other (9%). Minimum inhibitory concentration (MIC) values of tigecycline were determined by E test method (bio-Merieux, France). Tigecycline was active against all the *E. coli* and *Klebsiella* spp. strains included to the study, sensitivity rates were found to be 100% for both and MIC (50/90) values were 0.064/0.125 µg/mL and 0.5/0.75 µg/mL respectively.

Tigecycline may be an effective therapeutic alternative to carbapenems in infections caused by ESBL producing *E. coli* and *Klebsiella* spp. strains.

Key Words: *Escherichia coli*, *Klebsiella* spp. extended-spectrum beta-lactamase, E- Test, tigecycline



Investigation of Activity of Tigecycline Against Methicillin-Resistant Staphylococci Strains

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Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase negative staphylococci (MRCNS) are an important cause of infections worldwide. Vancomycin and other glycopeptide antibiotics are the current mainstay of therapy for infections caused by MRSA and MRCNS. However, the high prevalence of methicillin-resistant strains had led to increased use of vancomycin has resulted in the emergence of methicillin-resistant staphylococci with reduced susceptibility to glycopeptides. Treatment options for infections due to MRSA with reduced susceptibility to vancomycin are limited. Tigecycline could be an initial therapeutic alternative against MRSA and MRCNS.

The aim of this study was to determine in vitro activity of tigecycline against methicillin-resistant staphylococci strains isolated from various clinical specimens. Of all the 85 methicillin-resistant staphylococci strains 35 (41%) were identified as *S. aureus* and 50 (59%) coagulase negative staphylococci by using conventional methods. Thirty (35%) of them were isolated from outpatients and 55 (65%) from in patients. Methicillin resistance were determined and evaluated according to Clinical and Laboratory Standards Institute (CLSI) instructions by using disc diffusion method. Minimum inhibitory concentration (MIC) values of tigecycline for isolated strains were detected with E-test. (bioMerieux Marcy l'Etoile, France). MIC values of tigecycline for the 35 MRSA isolates were MIC₅₀: 0.094 µg/mL, MIC₉₀: 0.5 µg/mL) and for the 50 MRCNS isolates were MIC₅₀: 0.047 µg/mL, MIC₉₀: 0.25 µg/mL. All isolates (100%) were found to be sensitive to tigecycline.

The results of this study showed that tigecycline has very good in-vitro activity against both MRSA and MRCNS isolates.

Key Words: Methicillin-resistant *Staphylococcus aureus*, methicillin-resistant coagulase negative staphylococci E-test, tigecycline



Colistin Usage in Infections due to Multidrug Resistant Microorganisms: Clinical and Microbiological Response, Toxicity

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INTRODUCTION: Recently, life-threatening nosocomial infections caused by multidrug resistant gram-negative microorganism is increasing. Colistin has gain an important place in clinical practice for salvage therapy of these infections. In this study the patients who had been administered colistin was evaluated retrospectively regarding clinical and microbiological efficacy and toxicity.

METHODS: The study was conducted in Ankara Ataturk Training and Research Hospital. Clinical efficacy was defined as resolution of infection. Microbiological response was defined as eradication of microorganism from clinical sample obtained in 10 days after first colistin dosage. Nephrotoxicity was defined as a serum creatinine increase to 2 mg/dL or greater in patients with baseline serum creatinine less than or equal 1.3 mg/dL, or an increase greater than or equal to 50% in baseline serum creatinine clearance when it was already greater than 1.3 mg/dL or need for dialysis.

RESULTS: Thirty-six patients treated with colistin for nosocomial infection caused by MDR organisms were included in the study. The most frequent site-specific infection was ventilator-associated pneumonia (75%). Responsible microorganisms were identified as *Acinetobacter baumannii* in 34 patients and *Pseudomonas aeruginosa* in 2 patients. Clinical efficacy and microbiological response was achieved in 21 (58.3%) patients. Nephrotoxicity frequency was found as 30.6%. Concomittant nephrotoxic agent usage (27.2%) was found higher in the patients who had nephrotoxicity than the patients who had not (%8).

CONCLUSION: Nosocomial infections due to MDR gram-negative microorganisms can be effectively treated with colistin. Administration of concomittant nephrotoxic drugs seem to increase nephrotoxicity rates due to colistin.

Key Words: Colistin, *Acinetobacter*, nephrotoxicity



Comparison of Routine Laboratory Methods for Detection Methicillin-Resistant *Staphylococcus aureus*

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is major human pathogen wich has become a worldwide concern owing to increasing frequency in hospital-acquired and community-acquired infections. PCR amplification of the *mecA* gene is currently considered the gold standard for detection MRSA strains. But in routine laboratory practice, several phenotypic methods are used for determination these strains. However, detection is complicated by the fact that there are low level strains of MRSA and borderline-resistant *S. aureus*. We're going to use oxacillin and cefoxitin disk diffusion test, amoxicillin-clavulanate and ampicillin-sulbactam disk diffusion test, cefinase test for detection of beta-laktamases, E test and detection PBP2a to differentiate types 50 isolates *S. aureus* in outpatients of Canton Sarajevo.

Key Words: Routine laboratory methods, MRSA, BORSA



Resistance Patterns of Nonfermentative Bacteria Isolated from Blood Cultures in an Intensive Care Unit of a Training Hospital in Turkey

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Blood-stream infections (BSI) caused by nonfermentative bacteria are an important reason of morbidity and mortality in intensive-care units. It is important to have data about antimicrobial susceptibilities and to choose appropriate empirical treatment regimens for reducing morbidity and mortality. The aim of this study was to evaluate susceptibility rates of nonfermentative bacteria isolated from blood cultures in a 1100-bed tertiary training hospital in Izmir, Turkey. A total of 138 strains isolated from blood cultures between January-December 2009 included in the study. Automated blood culture system (Bactec 9240, Becton-Dickinson) was used for isolation of bacterial strains from blood specimens. Identification and resistance tests was made by both conventional methods and automatised system (Phoenix 100, Becton-Dickinson) according to CLSI standards. Of the 138 bacterial strains, 75 (54.3%) of them were *Pseudomonas* species and 63 (45.7%) of them were *Acinetobacter* species. Resistance rates of *Pseudomonas* species were more than 40% for aztreonam, cefepime, ceftazidime, ciprofloxacin. Resistance rates of gentamicine 22%, piperacillin-tazobactam 18%, imipenem/ meropenem 16% and, amikacin 9%, respectively. Resistance rates of *Acinetobacter* species were more than 50% for ampicillin-sulbactam, piperacillin-tazobactam, cefotaxime, cefepime, amikacine, gentamicine, imipenem, meropenem, ciprofloxacin. There were no colistin resistance determined. These results suggest that rates of resistance is higher in our hospital. Monitoring of resistance patterns in nonfermentative bacteria isolated from intensive-care patients is important to initiate appropriate ampirical treatment immediately.

Key Words: Resistance patterns, nonfermentative bacteria, blood cultures, intensive care unit



Resistance Patterns of Gram-Negative Enteric Bacteria Isolated from Blood Cultures in a Training Hospital in Turkey

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The aim of this study was to evaluate susceptibility rates of gram-negative enteric bacteria isolated from blood cultures in a 1100-bed tertiary training hospital in Izmir, Turkey. A total of 197 strains isolated from blood cultures between January-December 2009 included in the study. Automated blood culture system (Bactec 9240, Becton- Dickinson) was used for isolation of bacterial strains from blood specimens. Identification and resistance tests was made automatised system (Phoenix 100, Becton-Dickinson). Of the 197 bacterial strains 135 (68%) of them were *Escherichia coli*, 37 (19%) of them were *Klebsiella* species, 9 (4%) of them were *Morganella morganii*, 16 (9%) of them were other gram-negative enteric bacteria. Extended-spectrum beta-lactamase (ESBL) was detected in 33% *E. coli* of and 40.5% of *Klebsiella* species. The resistance rates of *E. coli* strains were more than 50% for cefuroxime, ampicillin, gentamicine, trimethoprim-sulfamethoxazole, amoxicillin-clavulanate, cefazolin, aztreonam. Quinolone resistance was detected in 48% of *E. coli* strains. Of the 48% *E. coli* strains detected as resistant against ceftazidime, ceftriaxone and cefepime, respectively. Resistance rates were 39% for cefoxitin, 26% for piperacillin-tazobactam, 11% for amikacine, and 4% for imipenem, respectively. Resistance rates of *Klebsiella* species were 94% for ampicillin, 94% for cefuroxime, 81% for amoxicillin-clavulanate, 62% for cefazolin, 54% for gentamicine, 54% for cefepime, 54% for trimethoprim-sulfamethoxazole, 54% for aztreonam, 54% for ceftazidime, 45% for ceftriaxon, 27% for ciprofloxacin/levofloxacin and piperacillin/tazobactam, 18% for cefoxitin, 8% for amikacin, respectively. Resistance were not determined against imipenem, meropenem and ertapenem in *Klebsiella* strains.

Key Words: Resistance patterns, gram-negative enteric bacteria, blood cultures



Staphylococci Isolated from Blood Culture and Their Antibiotic Susceptibility in a Training Hospital in Turkey

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Staphylococci are in the first line among microorganisms which can cause septicemia. Following the change of the resistance pattern is useful method in empirical treatment choice.

To this purpose it is investigated the resistance pattern of staphylococci isolated from blood culture from patients which are hospitalized in our hospital. When growth is was detected in automatised systems bacterial identification is was done automatically or by conventional methods. Antibiograms are applicated according to CLSI 2009 standards. 440 methicillin sensitive coagulase negative staphylococci (MSCNS), 547 methicillin resistans coagulase negative staphylococci (MRCNS), 136 methicillin-sensitive *Staphylococcus aureus* (MSSA) and 63 methicillin resistans *S. aureus* (MRSA) stains are examined. MRSA strains were 92% resistant to erithromycin and ciprofloxacin, 80% resistant to gentamicine and clindamycin, 69% resistant to trimethoprim- sulfamethoxazole and rifampicine. MSSA strains were penicillin G, erythromycine, rifampicine, ciprofloxasin, trimethoprim-sulfamethoxazole to resistant respectively to 38%, 31%, 28%, 20%, 13%, 12%, 11% rate, 5% were resistant to gentamicine and clindamicine. MRCNS strains were erythromycin 69%, trimethoprim-sulfamethoxazole to 60%, ciprofloxasin 56%, clindamicin 54%, rifampicine 42%, gentamicine resistant to 41%. MSCNS the strains of erythromycin, penicillin G, trimethoprim-sulfamethoxazole, ciprofloxacin, clindamycine, rifampicine, gentamicine respectively 16%, 13%, 11%, 7%, 5%, 4%, 1% of the rates of resistance were found. There is not detected any resistance rate in teicoplanin, vancomycin and linesolide.

Key Words: Staphylococci, blood culture, antibiotic susceptibility



In Vitro Activity of Doripenem and Other Antibiotics Against Extended-Spectrum Beta-Lactamase Producing and Fluoroquinolone-Resistant Organisms

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The rising incidence of infections caused by extended-spectrum beta-lactamase (ESBL) producing *E. coli* and *K. pneumoniae*. Doripenem is the newest carbapenem antibiotic commonly used to treat these microorganisms. The objective of this study was to determine the in vitro activity of doripenem and other antibiotics against ESBL producing and fluoroquinolone-resistant organisms.

We tested 100 clinically significant (n= 70 *E. coli* and n= 30 *K. pneumoniae*) ESBL positive and fluoroquinolone-resistant organisms. Minimum inhibitory concentration (MIC) of the isolates were determined for doripenem and other antibiotics by the E-test method (AB, Biodisk, Solna, Sweden). Doripenem susceptibility of ESBL-producing and fluoroquinolone-resistant *E. coli* and *K. pneumoniae* clinical isolates were evaluated and compared to other antibiotics (meropenem, imipenem, ertapenem, piperacilline-tazobactam, cefepime, and ceftazidime). Susceptibility was assessed according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) and CLSI (Clinical and Laboratory Standards Institute) breakpoints.

Doripenem, meropenem, and ertapenem inhibited 99% of the ESBL-producing and fluoroquinolone-resistant *E. coli* and *K. pneumoniae* isolates at $\leq 1 \mu\text{g/mL}$. Susceptibility rates for imipenem, piperacilline-tazobactam, cefepime, and ceftazidime among this isolates were 97%, 58%, 6%, 30%, respectively.

As a result of study, doripenem is very active against ESBL-producing and fluoroquinolone-resistant *E. coli* and *K. pneumoniae* isolates. Its activity is similar to that of meropenem, ertapenem and imipenem.

Key Words: Antibiotic, extended-spectrum beta-lactamase, fluoroquinolone-resistant



TEM-63 ESBL Producing *Salmonella enterica* Serovar *Isangi* from Zimbabwe

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Despite a paucity of reliable data it is clear that non-typhoidal *Salmonella* is an emerging problem in several countries of sub-Saharan Africa. Extended-spectrum beta-lactamase (ESBL)-producing *Salmonella enterica* serovar *Isangi* has emerged as one of the commonest *Salmonella* serovars in the African continent.

In this study twenty three isolates of *S. Isangi* were investigated for antimicrobial resistance and genetic relatedness. E-test confirmed ESBL-production in 22 *S. Isangi* isolates. The typing of beta-lactamases has been detected by PCR and DNA sequencing identifying TEM-63 in all ESBL positive. *S. Isangi* isolates contained an identical 4.0 kb integron with the gene cassettes *arr2/cmlA5/blaOXA10/aadA1* conferring resistance to rifampin, chloramphenicol, ampicillin, and streptomycin, these isolates were additionally resistant to tetracycline, ceftazidime, nalidixic acid, gentamicin, aztreonam, and trimethoprim-sulfamethoxazole. Isolates harbored from 1 to 3 plasmids ranging in size from 60 to 150 kb, of *IncA/C* and *IncY* replicon type. Pulsed-field gel electrophoresis band pattern analysis revealed a predominant PFGE pattern and MLST identified a unique MLST profile ST 216. This shows that *S. Isangi* isolates from Zimbabwe are clonally related and within the same clonal cluster of the ESBL producer *S. Isangi* circulating in Africa. The resistance to quinolones in addition to ESBL and MDR represent a serious threat for antimicrobial management of patients infected with these strains, especially children and HIV patients.

Key Words: Non-typhoidal *Salmonella*, multi-drug resistance, Africa



An Assessment for *Proteus* Strains Isolated from Clinical Specimens

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The rates of antibiotic resistance in common pathogenic bacteria as *Proteus* species have been increasing due to high and unnecessary antibiotic use, and it can vary according to geographical and regional location. In spite of this, little is known about the epidemiology of antibiotic resistance *Proteus* species in our region. The aim of this study is to assess the antimicrobial susceptibility of *Proteus* species produced from samples which sent to our laboratory from different clinics in our region.

For isolation of the strains, conventional culture methods were applied, to identify and obtain resistance to antimicrobial agents' disc diffusion and automatic commercial systems were used.

Of total 143 *Proteus* strains isolated from clinical samples, 81 from urine, 48 from wound, 7 from tracheal aspiration materials and 7 from blood samples were isolated. Antimicrobial susceptibility for these strains were determined to 99.3% for meropenem, 96.2% for imipenem, 95.1% for amikacin, 89.5% for cefepim, 86.0% for ciprofloxacin, levofloxacin, cefotaxime, ceftriaxone, 79.7% for gentamicin and 77.6% for amoxicillin-clavulanate.

In this study we reported that the findings related antimicrobial susceptibility for *Proteus* spp. in our region. We believe that these findings will be reference for new studies.

Key Words: *Proteus*, antimicrobial susceptibility



Evaluation of Drug Resistance Frequency Among *Enterococcus faecium* and *Enterococcus faecalis* Strains and Detection of *vanA/B* Genes in Vancomycin Resistant Isolates by PCR Method

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OBJECTIVES: Enterococci with various levels of resistance to vancomycin and other antimicrobial agents are now reported with increasing frequency from all over the world. *vanA* and *vanB* genes are associated with inducible high level resistance to vancomycin among enterococci. In this study, drug resistance frequency among *Enterococcus faecium* and *Enterococcus faecalis* was evaluated and *vanA/B* genes in vancomycin resistance isolates were detected by PCR.

METHODS: The disk diffusion antimicrobial susceptibility tests of 180 enterococcal hospital isolates by used 13 different antibiotics was determined according to CLSI procedures. The minimal inhibitory concentration (MIC) was determined for vancomycin resistance isolates by the E test strips. PCR was used for detection of *vanA* and *vanB* genes.

RESULTS: Between all of 180 totals enterococcal hospital isolates, 128 cases were *E. faecalis* and another isolates were *E. faecium*. The rates of resistance to antibiotics were determined as follows: erythromycin (61.1%), ampicillin (59.4%), gentamicin (2.2%), cefotaxime (18.3%), vancomycin (8.3%), meropenem (5.5%), chloramphenicol (36.1%), streptomycin (31.1%), tetracycline (24.4%), lincomycin (14.4%), ticoplanin (21.1%), amikacin and ciprofloxacin (3.8%). MIC was more than 256 µg/mL for isolates resistance to vancomycin. The *vanA* gene was found in 12 isolates whereas the *vanB* gene was not detected in any isolates.

CONCLUSION: This study showed that wide spread use of erythromycin and ampicillin, increases the incidence of indicator bacteria resistance to this antibiotics. Besides, frequency of *vanA* among enterococci isolates is not common and just in 12 isolates *vanA* gene was found. Although *vanB* gene was not observed among any isolates.

Key Words: Enterococci, vancomycin, *vanA/B* genes



Tigecycline Treatment of Polymicrobial Hepatic Abscess Following ERCP

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INTRODUCTION: Pyogenic hepatic abscess is very rarely observed. The most common etiology is biliary tract pathologies. Etiology is commonly polymicrobial, and the enteric bacteria and anaerobes. Tigecycline in hepatic abscess has been used rarely in the English literature. Hepatic abscess treated with tigecycline is presented here.

CASE: A 71 years old patient with the complaints of high fever, nausea-vomiting and fatigue was hospitalized presumptive cholangitis. The patient had ERCP a week ago. Tigecycline was initiated. Multiple abscesses (the size of the largest was 31 x 36 mm and 30 x 40 mm) were detected by abdominal USG and dynamic CT at the right lobe of the liver. Firstly, subcapsular abscess was drained. ESBL(+) *E. coli*, *Enterococcus faecalis* and *Enterococcus faecium* were reproduced in exudate culture. At the third week of the treatment, it was detected by the control CT the abscess was regressed to 30 x 19 mm and other multiple abscesses were disappeared. Fifteen cc of pus was drained. No growth was observed in the culture. Oral administration was discontinued due to patient's nausea and vomiting during treatment. The blood transaminase levels and coagulation markers are increased. Antibiotic treatment has been completed in 7 weeks. Antibiotic treatment was discontinued because no abscess was detected in control USG.

CONCLUSION: Tigecycline is an antibiotic with broad effective spectrum, and can be used alone in polymicrobial hepatic abscess when *Pseudomonas aeruginosa* is not the etiology. In hepatic abscess, the abscess drainage with antibiotic therapy should be initiated, and the treatment duration should be long to prevent recurrences.

Key Words: Tigecycline, hepatic abscess



Daptomycin Lock Treatment in the Hemodialysis Catheter Colonized with MRSA

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INTRODUCTION: Treatment of infections associated with a catheter in which *S. aureus* is the etiology is difficult without catheter removal. We present here a success of daptomycin lock treatment by systemic administration in catheter related bacteremia due to *S. aureus*, without removing the hemodialysis catheter.

CASE: A 51 years old patient who undergone hemodialysis for permanent catheter admitted with the complaints of fever following dialysis. She had purulent discharge in catheter entrance and leukocytosis in peripheral blood. Catheter can not be removed because there was no other peripheral open vascular access. Vancomycin was initiated for the catheter infection. MRSA was identified in the blood culture and exudate. In the tenth day of vancomycin treatment, MRSA was identified in the peripheral and catheter blood cultures, and the vancomycin was changed to daptomycin. In fourteenth day of the treatment, the patient was discharged from hospital by her will. After two weeks, the patient was rehospitalized due to a bacterial episode. MRSA was identified again. Daptomycin was given for six weeks by systematic and catheter lock method (CLM). Sequential oral treatment has been continued with ciprofloxacin and rifampicin. The patient has not experienced any other bacterial episodes during six months and the catheter infection has not been recurred.

CONCLUSION: The safest solution for the catheter infections is to remove the catheter and to give an appropriate antibiotic when the etiology is *S. aureus*. CLM and systemic daptomycin for a long time may be a best rescue therapy if the catheter can not be removed.

Key Words: Daptomycin, antibiotic lock treatment, catheter infection, *S. aureus*



Molecular Analysis of Carbapenem Resistance in Extended-Spectrum Beta-Lactamase Producing Gram-Negative Blood Isolates

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OBJECTIVES: Carbapenemase producing *Enterobacteriaceae* has become a global public health concern. This study was aimed to evaluate the molecular mechanisms of carbapenem resistance in *Enterobacteriaceae* in a university hospital.

METHODS: A total of 210 ESBL positive *E. coli* and *Klebsiella* spp. isolates were tested for imipenem (IMP), meropenem (MER) and ertapenem (ERT) susceptibility. ESBL production was confirmed with combined disk diffusion test in combination with boronic acid (BA). Modified Hodge test was performed for carbapenemase detection. AmpC were screened by ceftioxin-BA and MBL by IMP + EDTA. Carbapenem resistant isolates were further investigated by PCR for *blaKPC*, *blaOXA* and *blaAmpC* genes.

RESULTS: IMP, MER and ERT resistance was 5.7%, 1.9% and 2.4%, respectively. Twenty-three isolates were non-susceptible to any of the carbapenems tested. Seven of these were ESBL negative with CTX/CLA and CAZ/CLA, however, six of them were found ESBL positive with the addition of BA to CTX/CLA. Three phenotypic KPC producers were negative for *blaKPC*. Phenotypic AmpC activity was present in three *K. pneumoniae* of which one was positive for *blaAMP*C. Two of these were also phenotypic KPC producers. Only one *K. pneumoniae* isolate resistant to all carbapenems with MICs > 256 µg/mL, showed phenotypic MBL, KPC and AmpC production, however, no related beta-lactamase genes were detected. Four isolates were positive for *blaOXA-1* and one for *blaOXA-10*.

CONCLUSION: Carbapenemase resistance in *Enterobacteriaceae* isolates in our center seemed to be mostly associated with OXA-type beta-lactamases. Confirmatory tests for carbapenemase detection should be included in routine susceptibility testing protocols and molecular methods can be applied when mandatory.

Key Words: Carbapenemase, *Enterobacteriaceae*



Tigecycline Related Acute Generalized Exanthematous Pustulosis

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AIM: To present a case of tigecycline related acute generalized exanthematous pustulosis (AGEP).

CASE: A 39-year-old male with ventilator-associated pneumonia caused by *Acinetobacter baumannii* was evaluated. His general condition was poor, and he has pustular eruption on the body for the last four days. It was understood from the detailed history that he had fever of 39.5°C/axillary for the last one week, and *A. baumannii* growth in the tracheal aspirate culture. Thus, tigecycline 50 mg intravenous twice daily had been started to patient for five days; and no other new drugs had been given in the last 15 days. Erythema appeared on the face and neck about 12 hours after the start of tigecycline and pustules appeared later. On dermatologic examination, there were numerous pustules on the face, neck and legs on the erythematous areas that tended to unite and did not display a follicular localization (Figure 1). No pathologies were found in the oral examination, and psoriasis and allergy were negative in his history. The punch biopsy was taken from the skin lesions of patient. Histopathologic examination revealed the subcorneal and intraepidermal pustules, widespread spongiosis, neutrophil and histiocyte infiltration around vessels in the papillary dermis and exocytosis of eosinophils (Figure 2). The patient was diagnosed with AGEP according to findings mentioned above. Tigecycline was stopped, and intravenous methylprednisolon 60 mg/day was administered. Patient full recovered after this treatment.

CONCLUSION: Tigecycline may lead to AGEP. This is the first case of AGEP to be reported due to tigecycline.

Key Words: Tigecycline, adverse effect, exanthematous pustulosis

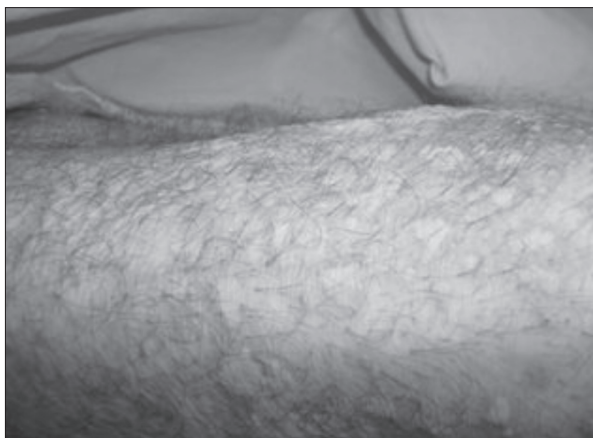


Figure 1. Erythema appeared on the leg.

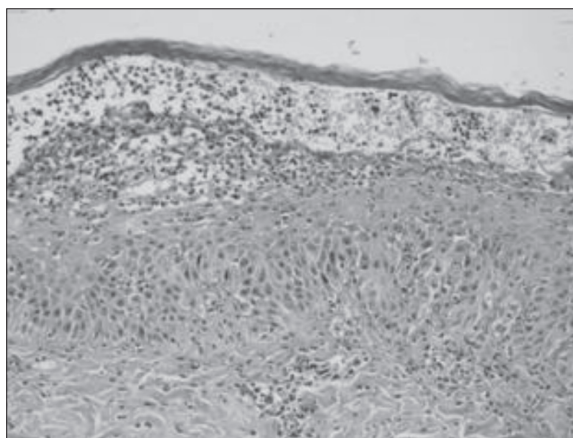


Figure 2. H&E x200, subcorneal and intraepidermal pustules, spongiosis, neutrophil and histiocyte infiltration around vessels in the papillary dermis and exocytosis of eosinophils.

Initial Treatment of HIV Infection in Antiretroviral-Naive Individuals in the Last Five Years in Istanbul, Turkey

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BACKGROUND: By April 2011, there are eleven individual or combination agents available for treatment of HIV infection in our country. These drugs are derived from three different classes (NRTIs, NNRTIs and PIs). This study aims to evaluate the initial treatment of HIV infection in antiretroviral-naive patients at a tertiary outpatient clinic in the last five years.

METHODS: Between January 2006 and December 2010, 195 HIV-infected patients were admitted to our center. One hundred and fifty antiretroviral-naive patients with CD4 cell counts below 350/ μ L were given first line antiretroviral therapy. Data about therapy were collected retrospectively from standardized HIV forms filled at admissions of the patients.

RESULTS: Eighteen in 2006, 23 in 2007, 36 in 2008, 40 in 2009 and 33 in 2010; in total 150 naive patients were given antiretroviral therapy. The allocation of preferred drug classes at the initial therapy can be seen by year in Figure 1.

As for 2NRTI, AZT + 3TC was used in years 2006, 2007 and until mid-2008. However, TDF + FTC has been preferred since its introduction in the country in May, 2008.

IDV and LPV/r of PI group are available in our country. 2NRTI + PI was used dominantly in 2006 and 2007. But since the introduction of EFV in May 2007, 2NRTI + NNRTI has been the first choice by the ratio of 83%. During the last two years, 2NRTI + PI and 2NRTI + NNRTI have been used with the proportion of 1:3 and 2:3 respectively.

CONCLUSION: Introduction of additional medicines that are proposed by international guides will enable us in Turkey to plan the appropriate treatment according to patients' characteristics.

Key Words: Initial, antiretroviral therapy, Turkey

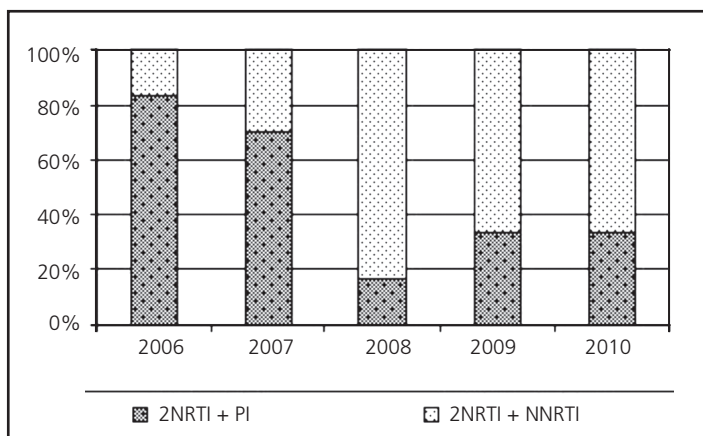


Figure 1. The drug classes preferred at the initial therapy.



Quality of Antibiotic Use in a University Hospital

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AIM: The misuse of antibiotics leads spreading of resistant microorganisms, increasing mortality and morbidity, adverse effects, and raising the cost. The aim of this study is revealing the quality of antimicrobial use at Dicle University Hospital (DUH) using a basic new scoring system as a quality indicator.

METHODS: Antibiotic use of inpatients was assessed with a prospective observational study in 2006. Using a standardized data collection form, the patients' data (clinic, epidemiology, laboratory and antibiotic use) was collected. At the same time, antibiotic use was assessed by an infectious disease specialist. An "infection assessment score (IAS)" was developed using basic clinical and laboratory findings. The score was tested for usefulness to make a decision of antibiotic indication.

RESULTS: In the prospective study, 1350 inpatients were evaluated that 461 (34.1%) of them were using antibiotic for treatment and 187 (13.9%) for prophylaxis. Antibiotic indication was found 355 (77.0%) of 461 patients in the treatment group. In 243 patients, antibiotic usage was completely accurate.

According to IAS, in 304 (65.9%) patients indication of antibiotic use was correct. The sensitivity of IAS was 84.2% and specificity was 95.3% for correct indication. All necessary laboratory tests were completed in 270 patients that IAS indicated antibiotic use in 229 (84.8%) of them. In that group, the sensitivity of IAS was 91.3% and the specificity was 95.1%.

CONCLUSION: The quality of antibiotic use is very important issue and we need more studies on that topic. Excessive surveillance studies are helpful for understanding the problem.

Key Words: Quality of antibiotic use, infection assesment score, audit of antibiotic use



Evaluation of Envirolyte as a Super-Oxidized Water (SOW) Against Multidrug Resistant Hospital Isolates Pathogens

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OBJECTIVES: Super-oxidized water (SOW) has been regarded as a new sanitizer in recent years. Production of SOW water needs only water and salt (sodium chloride). The aim of this study was to determine effectiveness of neutral SOW at killing of nosocomial pathogens and sporicidal activity.

METHODS: Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococcus (VRE) and multi-drug resistant (MDR) isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were selected as a MDR nosocomial pathogens for testing. In addition we used ATCC strains as a control strains. The sporicidal and antifungal activity of SOW also evaluated the efficacy of SOW to produce a reduction in at least 5 logs in viable cells counts regarded as bactericidal activity as recommended by UNE -EN standards.

RESULTS: According to EN1276, envirolyte had antimicrobial activity against ATCC organisms in both clean and dirty condition (albumin concentration 3 g/L) within one minute. This time was 5 minute for MDR organism in dirty condition. According EN 1650 Envirolyte showed antifungal activity against *Candida albicans* and spores of *Aspergillus niger* in clean condition. However at least 30 minute was need for killing spores of *Aspergillus niger* in clean conations. According to 14347 standards envirolyte was able killing of *Bacillus subtilis* spores in clean condition in five minutes.

CONCLUSION: In summary the finding of this study reveal that SOW is an effective disinfectant against a verity of organisms especially MDR and fungi. Envirolyte also was capable killing of spores of *B. subtilis*.

Key Words: Envirolyte, nosocomial pathogenes



Asystole After First Dose of Ceftriaxone: A Case Report

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INTRODUCTION: Ceftriaxone is a third generation cephalosporin commonly used for bacterial infections. Frequency of hypersensitivity skin reactions to ceftriaxone is between 1-3%, anaphylaxis is rare. To the best of our knowledge, the following case report is the first report of asystole to single dose ceftriaxone without previous exposure to ceftriaxone.

CASE: A 55 years old man was admitted to our emergency department because of high fever, abdominal pain, dysuria and weakness. There were not any histories of allergy or anaphylaxis. For fever etiology, blood and urinary cultures were taken. Then, 1 g ceftriaxone infusion was started slowly. Approximately one minute later cyanosis, hypotension, circulatory failure, respiratory failure and cardiac arrest were occurred. The rhythm was asystole. Cardiopulmonary resuscitation and tracheal intubation was performed immediately. Ceftriaxone infusion was stopped. Within 20 minutes the circulation was restored. The time of onset was in favour of ceftriaxone induced anaphylaxis. The patient was transported to the intensive care unit for further management. The patient was discharged good clinical condition on the 10th day of admission.

CONCLUSION: Emergency and infectious diseases physician should be aware of the possibility of anaphylaxis and asystole occurring with the first dose of ceftriaxone, and also receiving detailed informed patient consent, too.

Key Words: Asystole, ceftriaxone, adverse effect



Vancomycin-Induced Neutropenia in a Patient with Recurrent Bacterial Meningitis

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INTRODUCTION: Neutropenia and fever are rare adverse reactions to vancomycin therapy. Its mechanism is not completely clear but suggested to be immune-mediated.

CASE: An 18 year-old male was treated with intravenous vancomycin 2 g/day for recurrent bacterial meningitis which was resistant to ceftriaxon therapy. After vancomycin therapy, the symptom of meningitis was relieved. After 11 days with vancomycin therapy, he developed leucopenia (2200 mL/mm^3) and drug fever. His absolute neutrophil count decreased as 473 cells/mm^3 (23%). Despite an extensive laboratory and clinical evaluations, any reason for the neutropenia and fever were find. Vancomycin was discontinued at the 14th day of the treatment. His neutrophil level and fever returned to normal within two days.

CONCLUSIONS: Some reports showed that vancomycin-induced neutropenia typically occurs after at least 12 days of therapy and rapidly returns to normal generally within 2-5 days of discontinuation. Although current literature suggests vancomycin-induced neutropenia usually after 12 days of therapy clinicians should be keep in mind that it may occur earlier.

Key Words: Vancomycin, side effects, neutropenia, fever



In-Vitro Activity of Quinupristin/Dalfopristin and Methicillin Against *Staphylococcus* Strains Isolated from Clinical Samples

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OBJECTIVE: Resistance to antibiotics since the 1970s began to appear as a significant problem. In recent years, due to multiple drug resistance in gram-positive organisms, treatment of infections caused by gram-positive microorganisms has become more challenging. Quinupristin/dalfopristin is new parenteral antibiotics which was combination of two different compounds of streptogramin. They show their effects with binding to different region of bacterial ribosomes. They are effective against many gram-positive cocci including multiple-resistant *S. aureus* and *S. epidermidis*. In the study, to investigate susceptibility of 98 staphylococci strains isolated from clinical specimens to quinupristin/dalfopristin were aimed.

MATERIALS and METHODS: Ninety eight staphylococci strains including 74 CNS (coagulase negative staphylococci), 24 *S. aureus* strains which were isolated from various clinical specimens which had been sent to central laboratory of Kiziltepe State Hospital between February 2010-April 2011. Staphylococci were identified with conventional methods. According to "CLSI" criteria, sensitivity testing were performed by Kirby-Bauer disc diffusion method. *S. aureus* ATCC 25923 was used as the control strain.

RESULTS: 28% of the CNS were defined as MSCNS, 72% of the CNS were defined as MRCNS, 87% of *S. aureus* were defined as MSSA, 13% of *S. aureus* were defined as MRSA. 15% of MRCNS were resistant to quinupristin/dalfopristin, 5% of MSCNS were resistant to quinupristin/dalfopristin. In MSSA and MRSA strains resistance to quinupristin/dalfopristin weren't detected.

CONCLUSION: Staphylococci strains were found susceptible at high rates. Quinupristin/dalfopristin combination may be an alternative treatment for resistant gram-positive cocci infections.

Key Words: Quinupristin/dalfopristin, methicillin, *Staphylococcus*, susceptibility, streptogramin

Table 1. The distribution of resistance rate in *Staphylococcus* strains

[n (%)]	Quinupristin/dalfopristin (%)
MSCNS [21 (28)]	5
MRCNS [53 (72)]	15
MSSA [21 (87)]	0
MRSA [3 (13)]	0

MSCNS: Methicillin-susceptible coagulase-negative staphylococci, MRCNS: Methicillin-resistant coagulase-negative staphylococci, MSSA: Methicillin-sensitive *Staphylococcus aureus*, MRSA: Methicillin-resistant *Staphylococcus aureus*.



Antibiotic Resistance Rates of *Acinetobacter baumannii* Strains Caused Nosocomial Infection in Medical Intensive Care Unit

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INTRODUCTION: *Acinetobacter baumannii* causes severe hospital infections especially in intensive care units. This bacteria has become an important microorganisms in recent years and has been shown to increase morbidity and mortality. In this study, resistance rates of nosocomial *A. baumannii* strains to various antibiotics was investigated.

METHODS-RESULTS: We investigated 50 strains of *A. baumannii* which are isolated from patients in medical intensive care unit between 1 January 2010 to 31 March 2011. Of these specimens, 60% were tracheal aspiration material, 22% were blood, 18% were urine. The antibiotic resistance rates of the strains were found to be 100% for ceftriaxone, 96% for ceftazidime, 96% for cefepim, 76% for ampicillin-sulbactam, 62% for cefoperazone/sulbactam, 56% for imipenem, 64% for piperacillin/tazobactam, 54% for doripenem, 76% for amikacin, 80% for gentamicin, 78% for ciprofloxacin, 82% for trimethoprim-sulfamethoxazole, 18% for tigecycline, and 8% for colistin.

DISCUSSION: According to these results, colistin and tigecycline were the most sensitive antimicrobials against the *A. baumannii* strains isolated from our medical intensive care units. Antimicrobial resistance must be monitored for each hospital. This surveillance results might be useful for empirical treatment approach. In addition, because of increased frequency of multidrug resistant *Acinetobacter* infections, and a lack of new potent antimicrobial agent, the implementation of infection control measures seems to be the most effective way in preventing the spread of this infections.

Key Words: *Acinetobacter baumannii*, nosocomial infection, antibiotic resistance



An Evaluation of Antimicrobial Sensitivity Test Results from *Mycobacterium tuberculosis* Strains

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INTRODUCTION: Resistant *Mycobacterium tuberculosis* has become a major public health problem in recent years. For that reason, administration of the antimicrobial sensitivity test has become essential in order to determine appropriate methods of treatment in tubercular patients. Our study was intended to investigate the sensitivity to *M. tuberculosis* of isoniazid (INH), streptomycin (SM), rifampicin (RIF) and ethambutol (EMB), first choice drugs used in the treatment of tuberculosis.

METHOD: This study was a retrospective examination of patients monitored with a diagnosis of tuberculosis at the Ahi Evren Cardiovascular and Thoracic Surgery Training and Research Hospital in Trabzon-Turkey in January-December 2010. Patients' demographic characteristics, and results of antimicrobial sensitivity tests performed on *M. tuberculosis* strains growing in clinical specimens were analyzed. Isolate description and antituberculosis sensitivity tests were performed using the Mycobacteria Growth Indicator Tube (MGIT) 960 system.

RESULTS: Hundred thirty-four patients, 108 (80.6%) of whom were male, and *M. tuberculosis* isolates growing in clinical specimens taken from these patients were investigated. Patients' average age was 45.7 ± 17.9 . Resistance to at least one drug was determined in 28 (20.9%) isolates, and sensitivity to all drugs was determined in 106 (79.1%). Resistance levels in isolates were 17.2% (23/134) for isoniazid, 11.2% (15/134) for streptomycin, 4.5% (6/134) for rifampicin and 3.7% (5/134) for ethambutol. We also determined a 4.5% (6/134) level of multi-drug resistant strains characterized by isoniazid + rifampicin resistance, and 3.0% (4/134) isolates were resistant to four drugs.

CONCLUSIONS: The high levels of resistance we determined are similar to data for Turkey and developing countries. Because of these high resistance levels, culture and sensitivity tests must be performed on each patient before initiating tuberculosis treatment.

Key Words: *Mycobacterium tuberculosis*, antituberculosis treatment, antimicrobial sensitivity



ESBL Producing *Escherichia coli* and *Klebsiella pneumoniae* Strains Isolated from Urine of Nonhospitalized Patients in the Zenica-Doboj Kanton

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AIM: To determine the prevalence of ESBL - producing *E. coli* and *K. pneumoniae* strains isolated from urine of non-hospitalized patients during a two year period, to determine their distribution according to gender and age, as well as their antibiotic susceptibility to other groups of antibiotics.

METHODS: Identification of microorganisms was done by standard microbiological method and antimicrobial susceptibility was done according to CLSI standards. ESBL production was established by double-disk method and confirmed by E- test.

RESULTS: The prevalence of ESBL producing *K. pneumoniae* in year 2009. was 26.4%, and 34.6% in 2010. Prevalence of ESBL producing *E. coli* in 2009. was 2.8% and in 2010. it was 6,7%. Each strain showed different distribution according to the patient's gender and age. ESBL producing *K. pneumoniae* showed high resistance rates to gentamycin (69%), trimethoprim-sulfamethoxazole (81%) and quinolones (62%) in 2009. In year 2010 there was not considerable change in resistance excluding a decrease of resistance to quinolone (51%). ESBL producing *E. coli* showed also high resistance to gentamicin (54%), trimethoprim-sulfamethoxazole (64%) and quinolones (64%) in year 2009. In 2010 a decrease in resistance to quinolone was noticed (47%) as well as a rising resistance to trimethoprim-sulfamethoxazole (84%).

CONCLUSION: The increase of the isolates of both bacteria types is evident in 2010 in comparison with 2009. ESBL producing isolates of *K. pneumoniae* and *E. coli* in the period of examination showed approximately the same susceptibility to other nonbeta-lactaminic antibiotics.

Key Words: UIT, resistance, ESBL species



The Role of Education of Taking Blood Culture in the Bacteremia: An Example of a Government Hospital and Evaluation of Results

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The aim of this study is to reveal results of the education about the importance of taking blood cultures from patients and to review the status of resistance and agents of bacteremia changing with years in our hospital.

In this study, we evaluated the blood cultures from the patients monitored by various clinics in our hospital, between January 2005-December 2010. Because of blood cultures were monitored with manual system the records could not be reached between 2005-2007. Since then the doctors and nurses have been educated about the importance of blood cultures. The samples were evaluated by BacT/Alert Blood Culture System between 2008-2010. The organisms detected in positive cultures were identified by conventional methods. Antibiotic sensitivity tests were performed by disk diffusion method.

The sensitivity of blood culture was seen formed in clinics of our hospital at the end of education. While 16 at the first year, 2465 blood cultures were taken at the fifth year. Microorganism were isolated in 765 (19.1%) of. While the most frequently isolated coagulase-negative staphylococci as gram-positive, it was followed by *Staphylococcus aureus*. When the antibiotic sensitivity was investigated, the oxacillin resistance among coagulase-negative staphylococci was 58%. The most frequently isolated *Enterobacteriaceae* species as gram-negative and carbapenem was found to be the most effective antibiotic against the *Enterobacteriaceae* species.

The numbers of blood cultures were increased by staff education. To consider this cultures results before starting an empirical antibiotic therapy will help the clinicians.

Key Words: Blood cultures, causative organisms, antibiotic sensitivities



Investigation of In Vitro Activity of Fosfomycin Against *Enterobacteriaceae*

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INTRODUCTION: Members of *Enterobacteriaceae* have now emerged as a major problem in hospitalized patients. These organisms cause to many different infections, such as urinary tract infection, septicemia, intraabdominal and brain abscess, hospital-acquired pneumoniae, device-related infections. These microorganisms could show resistance to many antibiotics especially in hospitalized patients. Fosfomycin has a bactericidal activity by inhibiting the biosynthesis of peptidoglycan layer of the cell wall. Fosfomycin has activity against both gram-positive and gram-negative bacterias. It uses generally for the noncomplicated urinary tract infections. The aim of this study was to determine the efficacy of fosfomycin to *Enterobacteriaceae*.

MATERIALS and METHODS: This study included 100 *Enterobacteriaceae* (40 *Escherichia coli*, 30 *Klebsiella* spp., 30 *Enterobacter* spp.). The identification of the bacterial isolates was done by Vitek2 system (Biomérieux, France) and BD Phoenix (USA). The disc diffusion method was performed for the according to the CLSI (2010) by using discs 200 µg/mL fosfomycin added to 50 µg/mL D-glucose-6 phosphate (HIMEDIA, India).

RESULTS and DISCUSSION: The results of disc diffusion of fosfomycin were evaluated according to the CLSI (2010) criteria for *E. coli*. We have some difficulties for interpreting the results of isolates especially *Klebsiella* spp., *Enterobacter* spp. While measuring inhibition zone we have seen double zone image. Because of this we cannot decide the susceptibility of these isolates. In *E. coli* 39 of 40 isolates were susceptible to fosfomycin. Fosfomycin could be an alternative agent for the *Enterobacteriaceae*. There is need to new researchs for evaluating efficacy of fosfomycine against *Enterobacteriaceae*.

Key Words: *Enterobacteriaceae*, fosfomycin

Comparison of the In Vitro Susceptibility of *Haemophilus influenzae* Strains to Various Antimicrobial Drugs

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INTRODUCTION: *Haemophilus* species are members of the normal flora in the human upper respiratory tract. *Haemophilus influenzae* is commonly found in the throats of healthy individuals. Besides the early diagnosis and treatment of these cases, serious infections and possible complications can be prevented with appropriate empirical treatment. In this study, we aimed to determine the frequency and antimicrobial susceptibility pattern of *H. influenzae* strains isolated from clinical samples between 2005 and 2010.

MATERIALS and METHODS: The specimens from the outpatients and inpatients in Ondokuz Mayıs University, Medical Faculty Hospital between 2005 and 2010 were inoculated onto routine culture media (5% sheep blood agar, EMB agar and chocolate agar). After incubation at 37°C for 18-24 hours, microorganisms were evaluated according to their colony morphologies and staining characteristics and identified by BBL Crystal AutoReader (BD Diagnostic Systems USA) and Vitec 2 Compact (bioMérieux SA France) automated system. Antibiotic susceptibility tests were performed according to the standards of CLSI for *H. influenzae* strains.

RESULTS: The number of *H. influenzae* strains isolated from clinical specimens sent to the laboratory was 158. The annual resistance pattern of *H. influenzae* are presented in Table 1.

CONCLUSION: In our study, most of the clinical isolates were found to be resistant to trimethoprim-sulfamethoxazole and ampicillin. The rates of resistance to many other beta-lactams, chloramphenicol and tetracycline are lower. For patients with preliminary diagnosis of lower respiratory tract, given these resistance rates, we suggest that trimethoprim-sulfamethoxazole and ampicillin are not appropriate options. We suggest that determination of the isolation frequency of *H. influenzae* from clinical samples and its antibiotic susceptibility pattern may produce data for epidemiological studies and guide empirical antibiotic treatment.

Key Words: *Haemophilus influenzae*, resistance, empirical antibiotic treatment

Table 1. Annual resistance status of *H. influenzae* to some antibiotics

Years/Antibiotic (n,%)	AM	SXT	CAZ	C	MEM	IMP	CXM	AZT	TE	CIP	RA
2005											
14 (8.8)	1 (7.1)	4 (28.5)	1 (7.1)	0	0	0	0	1 (7.1)	0	0	1 (7.1)
2006											
15 (9.4)	1 (6.6)	1 (6.6)	0	0	0	0	0	0	0	0	0
2007											
47 (29.7)	5 (10.6)	10 (21.2)	1 (2.1)	0	0	0	0	2 (4.2)	4 (8.5)	0	1 (2.1)
2008											
35 (22.1)	6 (17.1)	12 (34.2)	3 (8.5)	2 (5.7)	0	0	0	0	0	1 (2.8)	0
2009											
30 (18.9)	9 (30)	12 (40)	0	1 (3.3)	0	0	0	0	0	0	0
2010											
17 (10.7)	0	7 (41.1)	1 (5.8)	0	0	0	0	0	0	0	0
Total 158	22 (13.9)	46 (29.1)	6 (3.7)	3 (1.8)	0	0	0	3 (1.8)	4 (2.5)	1 (0.6)	2 (1.2)

AM: Ampicillin, SXT: Trimethoprim-sulfamethoxazole, CAZ: Ceftazidime, C: Chloramphenicol, MEM: Meropenem, IMP: Imipenem, CXM: Cefuroxime, AZT: Aztreonam, TE: Tetracycline, CIP: Ciprofloxacin, RA: Rifampicin.



Investigation of In Vitro Activity of Fosfomycin Against Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Resistant Coagulase-Negative Staphylococci

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INTRODUCTION: *Staphylococcus aureus* is one of the important cause healthcare-associated bacteremia while it is leading bacterial cause of skin, soft tissue and bone infections. Coagulase-negative staphylococci are one of the most causative agent of bloodstream and central venous catheter related bloodstream infections among patients with hematology and oncology problems. All of the methicillin-resistant staphylococcal strains have acquired staphylococcal cassette chromosome *mec* (*SCCmec*) in their genome that carries the methicillin-resistance gene and other antibiotic resistance determinants. While beta-lactam antibiotics cannot use in the treatment of the methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCNS) infections glycopeptide antibiotics are first-line drugs for the treatment. But as we know there are some *S. aureus* strains that have vancomycin resistance. There is need to new drugs for the treatment of MRSA and MRCNS infections. Fosfomycin has a bactericidal activity by inhibiting the biosynthesis of peptidoglycan layer of the cell wall. Fosfomycin has activity against both gram-positive and gram-negative bacteria. It uses generally for the noncomplicated urinary tract infections. The aim of this study was to determine the efficacy of fosfomycin to the clinical isolates of MRSA and MRCNS.

MATERIALS and METHODS: This study was included 40 MRSA and 40 MRCNS clinical isolates. The identification of the bacterial isolates was done by Vitek2 system (Biomérieux, France) and BD Phoenix (USA). The disc diffusion method was performed for the according to the CLSI (2010) by using discs 200 µg/mL fosfomycin added to 50 µg/mL D-glucose-6 phosphate (HIMEDIA, India).

RESULTS and DISCUSSION: The results of disc diffusion for fosfomycin were evaluated according to the CLSI (2010) criteria for *Enterococcus faecalis*. We have some difficulties for interpreting the results of MRSA and some MRCNS. While measuring inhibition zone we have seen great inhibition zones in MRSA and some MRCNS isolates but also we have seen colony growth in the inhibition zone area. Because of these we measured inhibition zone from the colonies. According to the these measured inhibition zones all of the isolates have found susceptible to the fosfomycin. Thus, fosfomycin could be an alternative agent for the MRSA and MRCNS infections. There is need to new researchs for evaluating efficacy of fosfomycin against MRSA and MRCNS.

Key Words: Fosfomycin, methicillin-resistant *Staphylococcus aureus* and methicillin-resistant coagulase-negative staphylococci



Investigation of In Vitro Activity of Fosfomycin Against Vancomycin Resistant Enterococci

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INTRODUCTION: Enterococci are the member of the normal intestinal human flora and they are responsible for infections especially urinary tract infections. Increasing antibiotic resistance affects the treatment of infections that cause by enterococci. Last decades, glycopeptid resistance has became one of the most important problem in the nosocomial infections. The first report of vancomycin resistant enterococci (VRE) was from UK in 1988. After then it was widely distributed across the world. Fosfomycin has a bactericidal activity by inhibiting the biosynthesis of peptidoglycan layer of the cell wall. Fosfomycin has activity against both gram-positive and gram-negative bacterias. It uses generally for the noncomplicated urinary tract infections. The aim of this study was to determine the efficacy of fosfomycin to the vancomycin resistant enterococci.

MATERIALS and METHODS: This study included 62 vancomycin resistant enterococci that were collected by infection control committee for screening of the carriers in our medicine school teaching hospital. The identification of the bacterial isolates was done by Vitek2 system (Biomérieux, France) and BD Phoenix (USA). All of the VRE isolates were identified as *Enterococcus faecium*. The disc diffusion method was performed for the according to the CLSI (2010) by using discs 200 µg/mL fosfomycin added to 50 µg/mL D-glucose-6 phosphate (HIMEDIA, India).

RESULTS and DISCUSSION: All of the isolates that were tested found susceptible to fosfomycin according to the CLSI (2010) criteria for *Enterococcus faecalis*. VRE is one of the leading causative agent of nosocomial infections. The lackage of the antimicrobials for using the treatment of VRE infections is a problem. Fosfomycin could be used for all of the VRE infections other than urinary tract infections.

Key Words: Fosfomycin, vancomycin resistant enterococci



Distribution of Microorganisms Isolated From Wound Infections and Retrospective Investigation of Their Antibiotic Susceptibilities

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INTRODUCTION: Wound infections consist of pressure sores, nosocomial surgery sites, post-trauma, animal bites, burns and diabetic foot. These infections are presented with various clinical manifestations. Most of nosocomial wound infections appears to be still a serious problem. In this study, we aimed to investigate the distribution and antibiotic susceptibility of the microorganisms that had been isolated from wound samples that had been sent from various clinics to Microbiology Laboratory, Medical School, Ondokuz Mayıs University, Samsun.

MATERIALS and METHODS: Wound samples that had been sent from various clinics to our laboratory between January and December 2010 were cultured onto routine culture media and incubated under proper conditions. After incubation, traditional methods and Vitek 2 Compact (bioMérieux-SA France) automated system were used for identification and antibiotic susceptibility testing of the microorganisms. Confirmation and interpretation of the resistant strains were done according to recommendations of CLSI. Repeated isolates were excluded from the study.

RESULTS: A total of 621 strains were isolated from 448 clinical samples in one-year period between January and December 2010. Samples were from general surgery, plastic surgery and internal medicine in order of frequency. Distribution of the microorganisms was as the following; 125 (20.1%) *E. coli*, 108 (17.3%) *P. aeruginosa*, 75 (12%) *S. aureus*, 63 (10.1%) *A. baumannii*, 60 (9.6%) *Klebsiella* spp., 42 (6.7%) *Enterococcus* spp., 37 (5.9%) coagulase-negative staphylococci, 36 (5.7%) *Enterobacter* spp., 20 (3.2%) *Proteus mirabilis*, 15 (2.4%) *M. morgani*, 11 (1.7%) *Proteus vulgaris* and *S. marcescens*, 4 (0.6%) *Candida* spp. and *C. freundii*, 3 (0.4%) *A. faecalis*, 2 (0.3%) *B. cepacia*, *A. hydrophila* and *S. maltophilia* and 1 (0.1%) *P. stuartii*. Imipenem and meropenem resistance weren't observed in the *Enterobacteriaceae* strains. Imipenem and meropenem resistance were found in 22 (20.3%) and 20 (18.5%) *P. aeruginosa* strains, respectively. 50 (79.3%) *A. baumannii* strains were found to be resistant to imipenem and meropenem. Methicilline resistance was detected in 14 (18.6%) *Staphylococcus aureus* strains and 27 (72.9%) coagulase-negative strains. Resistance rates in *Enterococcus* spp. strains were as the following; penicillin 31 (73.8%), vancomycin 4 (9.5%), high-level gentamicin (HLGN) 15 (35.7%) and high level streptomycin (HLSM) 20 (47.6%).

CONCLUSION: In our laboratory, the most isolated bacteria were *E. coli*, *P. aeruginosa*, *S. aureus*, *A. baumannii*, *Klebsiella* spp., *Enterococcus* spp., CNS and *Enterobacter* spp., respectively. Given the susceptibility pattern of *E. coli* isolates, it was thought that it could be caused by the endogen flora of individuals. *Enterococci* may be resistant to many antimicrobial agents that are in use today. It is very difficult to eradicate these bacteria from hospitals colonized by resistant enterococci strains. As conclusion, we suggest that it is necessary to put emphasis on rational antibiotic therapy not to increase the rates of antibiotic resistance in microorganisms.

Key Words: Wound infections, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, staphylococci, methicillin resistance



Antibiotic Susceptibility Pattern of *Acinetobacter baumannii* Strains Isolated From Respiratory Samples

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INTRODUCTION: In this study, it's aimed to investigate the activities of tigecycline, doripenem and colistin to *Acinetobacter baumannii* strains isolated from respiratory samples in our hospital.

MATERIALS and METHODS: 50 *Acinetobacter baumannii* strains isolated from respiratory samples (tracheal aspirate and sputum) between January 2010 and June 2010 were included in this study. Identification of the strains was performed by BD Phoenix (Becton-Dickinson, USA) and Vitek 2 (Biomerux, France) automated system. Antibiotic susceptibility testing of the organisms was performed by broth microdilution method according to the recommendations of CLSI.

RESULTS: Of these 50 strains, 18 (36%) were from intensive care unit, 14 (28%) were from chest diseases, 6 (12%) were from cardiology and 12 (24%) were from other wards. 11 (22%) samples were sputum and 39 (78%) were tracheal aspirate. Of these 50 strains, 44 (88%) were resistant and 6 (12%) were susceptible to doripenem (EUCAST, version 1.3). The MIC₅₀ and MIC₉₀ values of tigecycline and colistin in 50 *A. baumannii* strains are given in Table 1.

CONCLUSION: Increasing resistance to the agents used in the treatment of infections caused by *A. baumannii* has become a major health problem worldwide and in our country. Because of the increasing resistance rates, the use of alternative drugs alone and in combination may be beneficial in treatment.

Key Words: *Acinetobacter baumannii*, antibiotic susceptibility, tigecycline, colistin, doripenem

Table 1. The MIC₅₀ and MIC₉₀ values of tigecycline and colistin in 50 *Acinetobacter baumannii* strains

	MIC ₅₀ (µg/mL)	MIC ₉₀ (µg/mL)
Tigecycline	1	2
Colistin	0.25	0.5



Comparison of the Activities of Vancomycin, Teicoplanin, Quinupristin/Dalfopristin, Linezolid and Daptomycin Against Staphylococci

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INTRODUCTION: Staphylococci have an increasing importance in nosocomial infections. In recent years, resistance to methicillin, vancomycin and teicoplanin has been increasing in staphylococci. Many new antibiotic choices have emerged in the treatment of nosocomial infections caused by staphylococci. In this study, we aimed to compare the activities of vancomycin, teicoplanin, quinupristin/dalfopristin, linezolid and daptomycin against strains of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCNS) that were isolated from nosocomial infections.

MATERIALS and METHODS: This study included 30 MRSA and 70 MRCNS strains isolated from tracheal aspirate and blood sample cultures in our laboratory between November 2010 and April 2011. Identification of the isolates was performed by Vitek 2 (Biomérieux, France) and BD Phoenix Automated Microbiology Systems (Becton Dickinson, USA). The minimum inhibitory concentration (MIC) values of vancomycin, teicoplanin, quinupristin/dalfopristin, linezolid and daptomycin against the strains were performed by E-test method (AB Biodisc, Sweden) according to the recommendations of the manufacturer.

RESULTS: The MIC₅₀ and MIC₉₀ values of the isolates are given in Table 1.

CONCLUSION: Many authors reported that MIC values of vancomycin and teicoplanin against staphylococci have increased. In our study we showed that the MIC₅₀ and MIC₉₀ values of daptomycin, linezolid and quinupristin-dalfopristin are lower than vancomycin and teicoplanin. The MIC₅₀ and MIC₉₀ values of vancomycin and teicoplanin have become close to the intermediate category. Therefore, close monitoring of the susceptibility patterns of these antibiotics in staphylococci would be appropriate.

Table 1. The MIC₅₀ and MIC₉₀ values of vancomycin, teicoplanin, quinupristin/dalfopristin, linezolid and daptomycin against MRCNS and MRSA strains

		Vancomycin	Teicoplanin	Quinupristin/Dalfopristin	Linezolid	Daptomycin
MRCNS (n= 70)	MIC ₉₀ (µg/mL)	2	8	0.38	0.5	0.38
	MIC ₅₀ (µg/mL)	1.5	3	0.19	0.25	0.125
MRSA (n= 30)	MIC ₉₀ (µg/mL)	1.5	4	0.75	1	0.25
	MIC ₅₀ (µg/mL)	0.75	2	0.25	0.5	0.19

Clinical Infectious Diseases

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Central Nervous System Brucellosis: Clinical Manifestations, Diagnosis and Treatment: Review of 18 Cases

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OBJECTIVE: In this study, we aimed to evaluate clinic features, diagnosis and treatment of patients with central nervous system brucellosis.

METHOD: Eighteen patients who referred to our department between 2005-2010 and diagnosed as neurobrucellosis were enrolled in this study. Clinical features and findings of blood culture, cerebrospinal fluid (CSF) culture, standard agglutination test, Coombs' test and CSF analysis were recorded for all patients, in addition to treatment and complications.

RESULTS: Some patients presented with neurological and psychiatric symptoms and signs. One of the patients was diagnosed with tuberculosis meningitis-neurobrucellosis co-infection and another case was diagnosed as post-treatment neurobrucellosis; remaining patients were considered as classical neurobrucellosis cases. While serum standart agglutination test (SAT) was negative in 4 patients, Coombs' test was negative in 2 cases. CSF SAT was found to be negative in 6 of the patients while coombs was negative in 4 patients. In one of the cases, all tests were negative except CSF Coombs' test. *B. melitensis* grew in blood cultures of one and CSF culture one patient. Treatment protocol in 11 patients was ceftriaxone + rifampicine + doxycycline for 4 weeks, followed by rifampicine + doxycycline 4 weeks. Alternative treatments were used in remaining patients. One patient death and mild sequel was present in another patient; remaining patients recovered without any sequel.

CONCLUSION: In differential diagnosis of unexplained neurological and psychiatric diseases in endemic areas for this disease, NB should always be considered. In order to prevent overlooking diagnosis, Coombs' test should be performed in CSF and blood.

Key Words: Neurobrucellosis, clinic, diagnosis, treatment

Table 1. Symptoms and findings of patients

Cases	Age	Sex	Symptom and findings
1	16	Female	Fever, headache
2	17	Female	Fever, headache, neck stiffness, depression, unconsciousness
3	23	Female	Headache, nausea-vomiting
4	23	Female	Headache, nausea-vomiting
5	24	Female	Fever, headache, vomiting, neck stiffness, unconsciousness
6	25	Female	Headache, aphasia, blurred vision, retrobulbar neuritis, neck stiffness, diplopia
7	26	Female	Fever, headache, unconsciousness
8	26	Female	Fever, headache, nausea-vomiting
9	28	Female	Headache, hemiparesis, aphasia, ataxia, facial paralysis, neck stiffness
10	30	Female	Fever, headache, personality disorder, neck stiffness
11	32	Male	Fever, headache
12	32	Female	Fever, headache, tremor in hands
13	34	Female	Fever, headache, dizziness, ataxi, diplopia, neck stiffness,
14	41	Female	Headache, nausea-vomiting
15	40	Female	Fever, headache, nausea-vomiting
16	44	Female	Fever, headache, depression
17	47	Male	Fever, pulmoner edema, hallucination, unconsciousness
18	68	Female	Fever, headache, polyarthritis



Has *Francisella tularensis* Persisted in a Region for 74 Years?

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In recent years, outbreaks of tularemia have increased in Turkey. In this study, features of a new outbreak occurred in a village close to the region where outbreaks of tularemia reported in 1936 were presented. The research team visited the village after the identification of index cases. Serum and throat samples were taken from 41 villagers were examined, and environmental samples were taken for identification of source of outbreak. *Francisella tularensis* was searched in these samples with culture, serology and molecular methods. In addition to the index case, 7 cases more were diagnosed as tularemia. All of cases had history of swimming in the pool filled with water from the stream, and the risk of contact with stream water was calculated to increase 9.3-fold. PCR analysis was positive in lymph node aspirate of the index case, home tap water of 3 cases, a spring water and stream water in the village. *F. tularensis* could not be isolated from any culture of samples. While tularemia has been not reported from Thrace Region of Turkey for 74 years, the disease reemerged in the region due to removal of hygienic measures. These clues may suggest that the agent continues its presence in the region for many years.

Key Words: *Francisella tularensis*, tularemia, water-borne diseases, Thrace Region of Turkey



Aetiological Characteristics of Pneumonia in Childhood

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AIM: To determine the characteristics of pneumonia in hospitalized children.

METHODS: We analyzed the epidemiological, etiological and clinical characteristics of pneumonia in 224 children hospitalized in one year period with a radiological proven pneumonia.

RESULTS: Almost half of children with pneumonia (46.4%) were infants, and 82.1% of patients were under five years. The boys were leading in all age groups. Pneumonia was bilateral in 102 (45.5%) patients, right sided in 100 (44.6%) and left sided in 22 (9.8%) patients. A significant number of patients had one or more predisposing factors (neurodevelopmental disorders, anemia, immunodeficiency). Clinical signs, gas analyses and pulse oximetry were in correlation and showing hypoxemic type of respiratory failure. In 100 patients (44.6%), admission C-reactive protein was above 10 mg/L. Leucocytes over $15 \times 10^9/L$ had 76 (33.9%) patients. Positive throat culture was in 47 patients, positive nasal culture in 41 patients and positive blood culture in 8 patients. The most frequently isolated pathogens were *Staphylococcus aureus*, *Klebsiella* spp. and *Pseudomonas aeruginosa*. Antibiotics received 92.5% of patients. All 224 patients had a positive outcome. The average length of intensive treatment was 2.8 days and average total length of treatment was 9.5 days.

CONCLUSION: The incidence of pneumonia was significant, especially in the infant age. Clinical signs, results of gas analysis and pulse oximetry are correlated well with radiological findings. Management of pneumonia in children must be in accordance with the general pediatric principles. Special attention should be paid to risk groups.

Key Words: Pneumonia, etiology, childhood

Table 1. The underlying risk factors for pneumonia

Risk factors	n (%)
Immunodeficiency	16 (7.1)
Anemia	100 (44.6)
Congenital heart defects	24 (10.7)
Neuromuscular disease	5 (2.2)
Neurodevelopmental disorders	28 (12.5)
Cystic fibrosis	1 (0.4)



A Case Report of Nosocomial *Providencia stuartii* Meningitis

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Providencia infections are very rare and usually they cause health-care associated infections. They mostly cause urinary-catheter-related infections. Meningitis associated with this bacteria is extremely rare. Here we report a *Providencia stuartii* meningitis in a patient with external lumbar drainage in a neurosurgery unit. A fifty-seven years old male patient was admitted to our neurosurgery department with head-ache and confusion. There was a subarachnoidal hemorrhagic on computerized tomography (CT) scan and he transferred to the intensive care unit. His neurological evaluation showed a grade 3a mental status according to the Yasargil classification and the Glasgow coma scale of 14. The CT-angiography and digital subtraction angiography revealed multiple arterial aneurisms. Three aneurisms were extracurriculated by coil embolization. Since the patient had hydrocephaly on his follow up on the 14th day, lumbar drainage (LD) was inserted. Daily cerebrospinal fluid (CSF) analysis were performed. On the 7th day of the LD the CSF findings revealed meningitis findings and *P. stuartii* was revealed from the CSF culture after 3 days. The LD was removed and daily lumbar punctures were performed. On the 7th day of his antibiotic therapy his laboratory findings returned to normal levels. Following CSF cultures were negative. The antibiotic therapy continued to 14 days. His meningitis was cured. The main infection associated with *Providencia* is nosocomial UTIs followed by bacteremia and pneumonia. Pericarditis and endocarditis cases were also reported. As to the authors' knowledge there are only two patients with *P. stuartii* meningitis in the literature and this is the third one.

Key Words: *Providencia stuartii*, nosocomial meningitis



Comparative Analysis of Cerebrospinal Fluid Adenosine Deaminase Activity in Meningitis

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AIM: The purpose is to determine cut-off value of adenosine deaminase (ADA) activity in cerebrospinal fluid (CSF) of patients with tuberculous and non-tuberculous meningitis and to assess its value in differential diagnosis.

MATERIALS and METHODS: CSF samples were treated and followed-up with a diagnosis of meningitis were enrolled in this study. The patients were 24 tuberculous meningitis (TBM), 25 purulent meningitis (PM), 25 aseptic meningitis (AM), and 17 neurobrucellosis (BM). ADA activity of CSF was quantified by colorimetric method.

RESULTS: In our study, mean ADA values in CSF were 28.34 ± 14.83 U/L in TBM cases, 8.71 ± 5.83 U/L in BM, 6.18 ± 2.54 U/L in PM and 3.43 ± 3.48 U/L in AM cases. When we accept CSF ADA activity cut-off value 12.5 U/L for differential of TBM and BM, its sensitivity was 92% and specificity was 88%. When we accept 12.35 U/L for differential of TBM and PM, its sensitivity was 92% and specificity was 100%. When we accept 6.45 U/L for differential of TBM and AM, its sensitivity was 100% and specificity was 92%. Additionally, we examined the cases dividing to two groups as TBM and non-TBM. When we accept ADA activity cut-off level 11 U/L for differential diagnosis of TBM and non-TBM by applying ROC analysing, its sensitivity was 92% and specificity was 90%.

CONCLUSION: The sensitivity and specificity for CSF ADA activity are considerably high in differential diagnosis of TBM from non-TBM. Hence CSF ADA activity may be used as a simple, cost-effective and reliable test for early differential diagnosis of TBM.

Key Words: ADA, CSF, non-tuberculous meningitis, tuberculous meningitis

Table 1. Demographic characteristics of patients

Meningitis	Men	Women	Total	Mean age \pm SD
TBM	10	14	24	34.2 ± 21.3
PM	10	15	25	32.6 ± 16.9
BM	9	8	17	40.1 ± 23
AM	15	10	25	26 ± 7.6
Total	44	47	91	32.2 ± 17.4

Table 2. Descriptive statistics and results for ADA in four groups

Meningitis	Mean	SD	95% CI	95% CI	Minimum	Maximum	p
TBM	28.34	14.83	22.0819	34.610	6.80	57.00	0.001
BM	8.71	5.835	5.7116	11.712	2.10	23.50	0.001
PM	6.18	2.54	5.134	7.234	2.10	11.40	0.001
AM	3.43	3.489	1.9919	4.872	0.80	14.80	0.001



The Evaluation of 105 Cases for Central Nervous System Infection

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AIM: To evaluate the agent pathogens, diagnosis, sequel and mortality rates in 105 cases followed for central nervous system (CNS) infections.

MATERIALS and METHODS: The records of patients that were followed for CNS infection between 2005 and 2010 were retrospectively analyzed. Forty five men and 60 women with ages ranging from 16 to 75 were included in the study.

RESULTS: Of the patients 35.2%, 22.8%, 14.2%, 14.2%, 13.3% had purulent meningitis, encephalitis, brucella meningitis, aseptic meningitis tuberculosis meningitis, respectively. Cultures were positive in 37.8% of purulent meningitis. *S. pneumoniae*, *Staphylococcus (S. epidermidis* in 3 cases and *S. haemolyticus* in one case) and *N. meningitidis* were isolated in 8 (57.1%), 4 (28.5%) and 2 (14.2%) cases, respectively. Ceftriaxone resistance was found in two of 8 isolated pneumococcus. Positive cerebro-spinal fluid culture rates in tuberculosis and brucella meningitis cases were 35.7% and 20%, respectively. Mortality-sequel rates were 20.8%/20.8% in viral meningitis, 18.9%/5.4% in purulent meningitis, 7%/42% in tuberculosis meningitis, 0%/6% in brucella meningitis while no mortality or sequel was seen in aseptic meningitis.

CONCLUSION: Since purulent meningitis and viral encephalitis are medical emergency, rapid and effective treatment must be immediately started. Vancomycin add-to treatment should be kept in mind due to increase of pneumococcus resistance to ceftriaxone. Tuberculosis and brucellosis must be considered in the differential diagnosis of CNS infections in our and developing countries.

Key Words: Meningitis, encephalitis, bacterial, aseptic, tuberculosis, brucella



A Rare Cause of Fever: Churg-Strauss Syndrome Related Omalizumab Treatment

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INTRODUCTION: Churg-Strauss syndrome (CSS) is a rare primary vasculitis with involvement of small and medium size arteries. CSS can be diagnosed by the presence of any four or more of the six criteria which include asthma, eosinophily, paranasal sinusitis, pulmonary infiltration, histological proof of vasculitis, and mono or poly neuropathy.

CASE: A 31 year-old male was hospitalized with fever, dyspnea and stomachache. His fever started during anti-Ig E (omalizumab) treatment for resistant asthma. He has been suffering from recurrent nasal polyps and asthma during the two years before his admission. Abdominal radiography and abdomino-pelvic ultrasonography were found normal. The laboratory examination showed eosinophilia (45%) and hyper IgE. In the third day, hyperesthesia and severe pain developed. This was diagnosed as polyneuropathy with EMG. In the following days, erythematous macules, papules and hemorrhagic vesicles appeared in the lower extremities. The histological examination of his skin biopsy showed wide-spread eosinophilic infiltration on the walls of vessel. Pulmonary infiltrates appeared on the chest radiography and thorax computerized tomography showed a ground glass appearance on right subpleural area. Colonoscopic biopsy revealed an eosinophilic leukocytes in the submucosal layers of the vessels. The patient was diagnosed as CSS. After two weeks hospitalization, high dose of IV corticosteroid (prednisolone 1 mg/kg) was started. Five days after, skin lesions regressed, level of eosinophily decrease less than %5 and fever declined.

CONCLUSION: Clinicians should be aware on CSS diagnosis in asthmatic patients when they apply to hospital with fever and dyspnea especially if they were under treatment with anti-IgE.

Key Words: Fever, Churg-strauss syndrome, omalizumab, corticosteroid treatment



Atrophic Rhinitis Positive with *Actinomyces naeslundii* in a Child Patient: Case Report

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Atrophic rhinitis is a rarely witnessed inflammatory and chronic infection characterized by the atrophy of nasal mucosa and conchas, nasal crusting with bad smell and the enlargement of the nasal space with paradoxical nasal congestion. Primary and secondary forms of atrophic rhinitis are well-established. While primary atrophic rhinitis occurs in a previously healthy nose, secondary form frequently occurs following extensive sinus surgery, nasal trauma and chronic granulomatous diseases. On the physical examination of the case during anterior rhinoscopy, common crust and purulent, yellowish-dark green discharge were determined in nasal cavity. *Klebsiella ozaenae* and *Staphylococcus aureus* in aerobic culture performed with automated bacteria identification and susceptibility testing system (Phoenix 100) and *Actinomyces naeslundii* in anaerobic culture were yielded. *A. naeslundii* was identified by using API 20 A and antibiotic susceptibility tests performed via E test method.

K. ozaenae was found to be resistant only to ampicillin and was susceptible all the other tested antibiotics: amikacin, amoxicillin/clavulanic acid, ampicillin/sulbactam, cefazolin, cefuroxime, ceftriaxone, cefepime, ciprofloxacin, gentamicin, imipenem, meropenem, piperacillin/tazobactam, trimethoprim-sulfamethoxazole; and expanded spectrum beta-lactamase (ESBL) was negative. *S. aureus* was found to be resistant to cefazolin, clindamycin, erythromycin, fucidic acid, meropenem, oxacillin, penicillin G and ampicillin; was susceptible to gentamicin, levofloxacin, moxifloxacin, ofloxacin, vankomycin, teicoplanin, tetracycline and trimethoprim-sulfamethoxazole. *A. naeslundii* was found to be resistant to metronidazole; susceptible to moxifloxacin and meropenem, beta-lactamase test was negative.

Presenting atrophic rhinitis in a 10-year-old male patient with clinical, microbiological and pathological features, the subject were discussed in the light of related literature.

Key Words: *Atrophic rhinitis, Klebsiella ozaenae, Actinomyces naeslundii*



Disseminated *Mycobacterium tuberculosis* Infection Involving Three Different Systems in an Immune-Competent Patient

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In this report, a case of extrapulmonary tuberculosis with miliary involvement affecting central nervous system and bone-skeletal system in a young immune-competent patient is presented.

CASE: Twenty-four year old male patient referred to emergency department with complaints of fever and loss of consciousness. Initial examination of the patient revealed an axillary temperature of 39°C, he was unconscious and lethargic. Generalized rales were found in both lungs. Neck rigidity was present and cranial CT showed hypodense lesion. Generalized millimetric nodular infiltration was observed in pulmonary radiography. Laboratory values were as follows; WBC: 13.000/mm³, sedimentation 90 and CRP was 4 mg/dL.

In cerebrospinal fluid (CSF), 500 leucocytes/mm³ was seen and CSF glucose was 8 mg/dL, concurrent blood glucose was 86 mg/dL and CSF protein was 132 g/dL.

Ceftriaxon therapy was initiated with the diagnosis of meningitis and pneumonia. Tuberculosis meningitis was considered for the patient who was found to be acit- stain (AFS) with the diagnosis positive. During the first 12 hours of treatment, anti-tuberculosis regime with isoniazid, rifampin, pyrazinamide, and ethambutol was added to ceftriaxone. Dexamethasone treatment of 4 mg x 4/day was initiated.

AFS was positive in sputum. Patient was diagnosed as miliary tuberculosis. Hip MR revealed findings in accordance with bone-joint tuberculosis.

Parenteral ceftriaxone treatment was administered for 21 days and he was discharged with full recovery and with recommendations, maintaining anti-tuberculosis treatment.

CONCLUSION: When extrapulmonary tuberculosis is detected, all systems should be screened for tuberculosis infection, while the primary focus is being searched.

Key Words: Extrapulmonary tuberculosis, tuberculosis meningitis, miliary tuberculosis, skeletal tuberculosis



Re-Evaluation of 400 Crimean-Congo Haemorrhagic Fever Cases in an Endemic Area

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BACKGROUND: Crimean-Congo haemorrhagic fever (CCHF) is a tick-borne viral disease, leading to death following a clinical syndrome of haemorrhagic fever. This trial is invaluable due to highest number of patients enrolled in a CCHF trial up to this date.

METHODS: This trial was conducted in Tokat State Hospital which is located in an endemic area. Four hundred patients referring to hospital between 2007-2009 and diagnosed as having CCHF with RT-PCR were enrolled in this trial. Ribavirin was not administered to any patient. Epidemiological, clinical and laboratory findings of CCHF and factors affecting mortality were evaluated.

RESULTS: History of tick bite was present in 337 (84.2%) patients, 20 (5%) patients died and 380 (95%) patients recovered. It was found that age, white blood cells, aPTT, ALT and AST values were significantly higher in patients who died, as compared to recovered cases and the difference was significant. Platelet values were significantly lower in patients who died, as compared to recovered cases. Laboratory values are shown in Table 1.

CONCLUSION: Use of ribavirin is not required in treatment of CCHF. Age, high levels of ALT, AST, WBC, aPTT, platelet levels and decrease in these values during follow-up are indicative of a poor prognosis.

In our area, CCHF remains to be an issue. Individuals residing in risky areas are prone to this risk, even though they may not refer with a history of tick bite.

CCHF should be considered in pre-diagnosis of every patient residing in risky areas and referring with fever, asthenia and pain symptoms.

Key Words: Crimean-Congo haemorrhagic fever, CCHF, ribavirin

Table 1. Comparison of demographic characteristics and laboratory values of deceased and recovered patients

	Convalescent (n= 380)	Exitus (n= 20)	p
Age, mean \pm SD	46 \pm 18	57 \pm 8	0.005
Male, N (%)	208 (55)	14 (70)	0.181
ALT IU/L median (IQR)	43 (25.5-84)	74 (47-155)	0.001
AST IU/L median (IQR)	73 (41-161)	199 (64-350)	0.002
WBC1 10 ³ / μ L median (IQR)	2700 (2000-3600)	4150 (3700-4800)	0.002
WBC2 10 ³ / μ L median (IQR)	2100 (1600-3000)	2750 (1500-4500)	0.473
Hemoglobin g/dL mean \pm SD	13.7 \pm 1.64	12.64 \pm 3.39	0.963
Platelet1 10 ³ / μ L mean \pm SD	98 \pm 48	65 \pm 40	0.000
Platelet2 10 ³ / μ L mean \pm SD	63 \pm 42	14 \pm 8	0.000
PT median (IQR)	11.15 (10-13)	13.1 (11-14.4)	0.035
PTT median (IQR)	37 (31-43)	52 (47-65)	0.000

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, WBC1: Initial white blood cell count on referral, WBC2: Lowest white blood cell count, Platelet1: Initial platelet value, Platelet 2: Lowest platelet value, PT: Prothrombine time, aPTT: Active tromboplastine time, SD: Standard deviation, IQR: Interquartile range.



Molecular Characterisation of Clinical (Inpatients/Outpatients) and Colonizing Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* in Bosnia and Herzegovina

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OBJECTIVES: To determine the antibiotic resistance and genetic background of methicillin-sensitive (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) obtained from various clinical specimens of inpatients, outpatients and carriers (healthy food handlers) in Bosnia and Herzegovina, during 2007-2009.

METHODS: *S. aureus* were isolated and identified using standard microbiological methods (coagulase and catalase tests), antibiotic susceptibility testing by disc diffusion method according to the CLSI guidelines. Methicillin resistance was confirmed by the presence of the *mecA* gene by PCR. The genetic characterization was performed using spa-typing.

RESULTS: *S. aureus* was isolated from 68/81/189 in-/outpatients/carriers samples, 46%/18%/2% of which were MRSA. Among 37/64/130 of in-/outpatient/carriers MSSA, 22/38/66 spa types, clustered into eight, nine and nine spa-CCs, two, three, and four no founders, respectively, and singletons noted. The main MSSA spa-CCs in all three settings were spa-CC015 associated with MLST CC45, 16%/21%/24%, respectively. Most MRSA associated with MLST 355/595 no founder clone (4), i.e. t355 spa type, 77%/43%/67%, respectively, which not found in MSSA isolates. MRSA-related background had 34%/46%/60% of in-/outpatients/carriers MSSA, respectively. There were 47%/97%/71% MSSA and 23%/29%/67% MRSA of in-/outpatient/carriers, respectively, sensitive to all antibiotics tested (the beta-lactam compounds excepted). Multidrug resistance (to three or more antibiotic groups) was found in 7% carrier MSSA, and in once in hospital/outpatient MRSA.

CONCLUSION: MSSA were more heterogeneous than MRSA. The prevalence of MSSA with MRSA-related background was lower in hospital than in outpatients and carriers, MRSA prevalence was highest in hospital isolates, suggesting that MRSA did not arise from predominant MSSA clones in hospital.

Key Words: MSSA, MRSA, spa-typing, MLST, antimicrobial susceptibility



A Case Report: Brucellosis with Acute Cholecystitis

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OBJECTIVE: Brucellosis is a zoonosis with serious complications that may affect all organ systems. Acute cholecystitis is a rare complication. In this case report, we present our experience of acute cholecystitis (AC) which is a part of brucellosis clinical feature.

CASE: A 57 year old male patient administered to general surgery department with stomachache, fatigue and fever. Physical evaluation revealed a tenderness at right upper quadrant and pain with abdominal defence which was accepted as acute abdominal syndrome. Abdominal ultrasound presented AC and splenomegaly. Thus, patient received cefobid (2 x 1 g/day intravenously) for cholecystitis. We examined this patient for by an infectious diseases consultation for continuing complains and fever over 39°C. By our examination, patient was alert/cooperated in a well consciousness. His body temperature was 39°C with abdominal defence and severe pain at right upper quadrant via palpation. Blood culture, Gruber-Widal test, Wright tests were planned. Results concluded (-) for Gruber-Widal, 1/640 (+) for Wright test titration. Thus, diagnosis accepted as brucellosis cholecystitis and splenomegaly. A treatment of doxycycline (2 x 100 mg/day) with rifampicin (1 x 600 mg/day, prior to nutrition) was administered. Body temperature returned to normal in 4 days, complains also lessened. At the seventh day of treatment, patient was discharged in a symptom-free state to complete his treatment at home. Doxycycline and rifampicin combination continued for 6 weeks. Control Wright test titration measured as 1/80 after medical treatment.

CONCLUSION: Brucellosis is endemic in Turkey. It also may arise atypically which becloud certain diagnosis. In acute cholecystitis, brucellosis should be a differential diagnosis.

Key Words: Acute cholecystitis, brucellosis



Listeria monocytogenes Meningoencephalitis: The Case Report

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Listeria monocytogenes is one of five most frequent causes of abscess meningitis with affinity for soft cerebral meninges and cerebral parenchyma. It rarely occurs in our region. The case of 43-year-old immunocompetent patient with severe *Listeria* meningoencephalitis is presented. Exterior ventricular drainage and ventricoperitoneal drainage were performed due to acute internal hydrocephalus. She was treated with double antibiotic and corticosteroid therapy during the whole period of hospitalisation. The outcome of the disease was lethal.

A treatment of *Listeria* meningoencephalitis requires antibiotic and corticosteroid therapy as well as neurosurgical intervention in some cases.

Key Words: *Listeria monocytogenes*, meningoencephalitis, ventricoperitoneal drainage



An Outbreak of Trichinosis in Tuzla

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Trichinosis, a zoonosis caused by a parasite whose natural reservoir are wild, domestic animals and rodents. Trichinosis is widespread throughout the world, mostly in the US, where over 20 million people are infected. In Canada 1% of people is infected, and in the countries of South America about one million inhabitants are infected. In Netherlands, Denmark and Belgium, trichinosis is eradicated. In Australia, there were no domicile cases of infection, but there were descriptions of imported trichinosis cases from Croatia. The first cases of trichinosis in Bosnia have been described in 1923. The aim of this work was to show an outbreak of trichinosis, caused by eating pork sausages, endemic area and severity of the disease. By retrospective analysis of medical records, we presented 8 patients with trichinosis, who have been hospitalized. Infested meat has been consumed by 30-40 persons. Of these, 8 were hospitalized, 9 patients with problems were returned to home treatment, and 6 persons were asymptomatic. From 8 hospitalized 5 (62.5%) were male and 3 (37.5%) females, aged 8-72 years. Symptoms in patients were reported 7-25 days after eating sausages. Fever had 8, rash 2, swelling of face and eyelids 4, muscle pain 8, diarrhea 3, eosinophilia 8 and increased CPK 8 patients. Ultrasonic examination of the heart was performed in 4 patients. Elisa test for trichinosis was performed in 5 patients, IgM antibodies were positive in 4 and IgG in 1 patient. All were treated with mebendazole and symptomatic therapy. All patients were cured.

Key Words: Trichinosis, prevalence, endemicity, pig



Analysis of 16 Cases with Tuberculous Meningitis

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INTRODUCTION: Tuberculous meningitis (TM), an extrapulmonary form, is a central nervous system disease which presents a rapid progression, higher mortality and permanent neurologic sequel. Thus, early diagnosis/treatment is particularly important.

OBJECTIVE: Hereby, we summarized our 16 cases of TM retrospectively with their medical history and clinical/laboratory features within the dates between 2002 to 2007.

RESULTS: Mean ages were 20-25 for 25%, 27-50 for 50% and over 50 for 25% of all cases. By their administration to our department, all patients presented neck stiffness (++++), Kernig (+) and Brudzinsky (+). In 8 cases (50%), patients reported their complains to onset two weeks or more before administration. Rest cases were within symptoms in the last 3 to 7 days. None of our patients were positive for prior tuberculosis findings.

TM diagnosis depended on cerebrospinalfluid BACTEC positivity in 8 (50%), cerebrospinal fluid ARB positivity in 5 (31.2) and cerebrospinalfluid lowenstein positivity in 1 (6.2%) case. In 1 other case (6.2%) we observed cerebral tuberculoma by cranial magnetic resonance imaging scans. On the other hand, we diagnosed 1 (6.2%) case by his cerebrospinal fluid findings, clinical features, medical history and response to specific treatment. We administered anti-tuberculosis treatment with four different drugs; isoniazid (1 x 300 mg), rifampicin (2 x 300 mg), pirazinamid (1 x 2000 mg) and etambutol (1 x 2000 mg). Furthermore, we applied mannitol (1 mg/kg/day for 3 days) and dexamethasone (4 x 8 mg intravenously for the initial day, reduced and ended gradually in 6 weeks). Four different antituberculosis treatment continued for three months. Afterwards, pirazinamid and etambutol were ceased. Isoniazid with rifampicin were, on the other hand, continued for 18 months.

CONCLUSION: All patients from the study group were cured completely without any neurological sequel.

Key Words: Tuberculous meningitis



Brucellosis Leptospirosis Co-Infection: A Case Report

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Brucellosis and leptospirosis are zoonoses, and are widespread throughout the world. A person becomes infected through direct or indirect contact with infected animals. These diseases are multisystemic and can be manifested with various clinical features. The aim of our study is to present a case of brucellosis and leptospirosis co-infection. A farmer 49 years old was admitted to our clinic with complaints of high fever, weakness, malaise, pain in muscles and bones of the lower extremities, difficult urination, red urine, red eyes, yellow skin, and pain in the testicles. These symptoms first appeared 10 days earlier. Physical examination on patient admission showed that the patient was febrile, with icteric skin, on skin of the abdomen was present petechial rash. Conjunctives were strongly injected. The throat was hyperemic with aphthous changes in soft palate. In the laboratory findings, there was a leukocytosis, thrombocytopenia, high bilirubin, and elevated CRP. ELISA test for leptospirosis and brucellosis were made, IgM antibodies were positive for both diseases. The patient was treated with antibiotics, symptomatic and supportive therapy. Patient's condition improved and was discharged to home care.

CONCLUSION: In Bosnia and Herzegovina these two diseases are a serious problem, particularly brucellosis. Therefore, it is necessary to pay more attention to prevention, appropriate treatment, and thus prevent the occurrence of complications.

Key Words: Brucellosis, leptospirosis, co-infection



A Healthcare-Associated Pneumonia Case Due to Colistin-Resistant *Acinetobacter baumannii*

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INTRODUCTION: *Acinetobacter baumannii* has become a serious nosocomial pathogen due to its broad antimicrobial resistance patterns in Turkey. Here a healthcare-associated pneumonia case due to pan-drug resistant *A. baumannii* is presented.

CASE: A 78 years old male was hospitalized with a diagnosis of encephalopathy. The patient had fever on the 28th day of hospitalization in intensive care unit. Increased and purulent respiratory secretion were detected. There was pulmonary infiltration on the right lung in the postero-anterior lung radiography. *Acinetobacter baumannii* ($\geq 10^5$ CFU/mL) that is resistant to the colistin was identified from endotracheal aspirate culture. The isolate was resistant to all other antibiotics except cefoperazone-sulbactam (intermediate) and tygecycline (MIC= 4 mg/L). Resistance of colistin was confirmed with E test. Colistin IV 2 x 150 mg and colistin inhaler 2 x 75 mg was combined with cefoperazone-sulbactam 2 x 2 g IV. Fever was not turn back to the normal and clinical and laboratory findings were not resolved on the third day of therapy. Tygecycline added to therapy although it was not approved for pneumonia. Antimicrobial therapy was stopped on 14th day. The patient is still in ICU because of encephalopathy and alive.

CONCLUSION: Synergism has been demonstrated between colistin and imipenem, rifampicin, cefoperazone-sulbactam and tygecycline. To take advantage of this synergic effect seems as most reasonable approach for the treatment of the patients infected with pan-drug resistant *A. baumannii*.

Key Words: *Acinetobacter*, pan-rezistant



Use of Entecavir After Reactivation of Hepatitis B Infection in Cancer Patients

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Patients infected with hepatitis B virus, which is common worldwide can have fatal reactivation following cytotoxic chemotherapy. The generally approved recommendation is the use of a preventive antiviral prescribed to HBsAg positive cancer patients.

We have two cases, the first of which is a severe HBV reactivation in a previously HBsAg negative patient who received a chemotherapeutic regimen for treatment of chronic lymphocytic leukemia (CLL), and who was successfully treated with entecavir, achieving a rapid and sustained suppression of HBV replication and developed anti-HBs.

The second case is a breast cancer patient who was HBsAg positive and had hepatitis B reactivation and was successfully treated with entecavir.

Key Words: Entecavir, hepatitis B, cancer

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OBJECTIVE: This study aims to evaluate the serum selenium (Se) status of patients with brucellosis, salmonellosis, pulmonary tuberculosis, chronic osteomyelitis, and sepsis, and to compare the results with healthy individuals.

METHODS: This study was performed from January 2005 to December 2007 at Dicle University Hospital. A total of 30 patients with brucellosis, 30 patients with salmonellosis, 25 patients with pulmonary tuberculosis, 20 patients with chronic osteomyelitis, 30 patients with sepsis, and 40 healthy individuals in the control group were included in the study. A 5 mL sample of venous blood was taken from the 175 study individuals. Serum Se levels were measured in all the serum samples using a Unicam 929 atomic absorption spectrophotometer. Statistical analysis was performed using SPSS version 16.0.

RESULTS: The mean age, male gender, and serum Se levels for the 135 study cases and 40 healthy controls, and their statistical results are presented in the Table 1. Statistically significant increases of serum Se levels were detected in patients with pulmonary tuberculosis, chronic osteomyelitis, and sepsis when compared with controls; and statistically significant decreases of serum Se levels were detected in patients with brucellosis when compared with controls. There were no statistically significant differences in serum Se levels for patients with salmonellosis when compared with controls. However, an increasing serum Se level was detected in patients with salmonellosis (Table 1).

CONCLUSION: The metabolic effects of alterations in serum Se levels among patients with such infectious diseases may be suitable for further investigative study.

Key Words: Selenium, infectious diseases, trace elements, serum

Table 1. The mean age, male gender and serum Se levels of 175 study individuals, and their statistical results

Diseases	Male n (%)	Mean age ± SD	Se ± SD (µg/dL)	p
Brucellosis	15 (50)	39.4 ± 12.7	66.1 ± 29.8	0.0001
Salmonellosis	15 (50)	40.1 ± 12.2	158.7 ± 121.7	0.08
PT	17 (68)	39.8 ± 18.1	189.4 ± 67.3	0.0001
CO	15 (75)	40.2 ± 16.1	336.4 ± 209.6	0.0001
Sepsis	15 (50)	54.6 ± 18.4	205.5 ± 106.5	0.0001
Controls	20 (50)	29.7 ± 8.1	120.1 ± 54.6	-

SD: Standard deviation, PT: Pulmonary tuberculosis, CO: Chronic osteomyelitis.



Seroprevalence of Hepatitis A Among Children Aged 1-16 Years in Eastern Anatolia, Turkey

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BACKGROUND: Hepatitis A may lead to severe clinical manifestations, including fulminant hepatitis among adults. This study aims to determine the seroprevalence of hepatitis A among children aged 1-16 years in Tunceli province.

METHODS: This study was conducted at Tunceli State Hospital in Eastern Anatolia, Turkey. Anti-HAV IgM and anti-HAV IgG antibodies were evaluated among 351 patients admitted to our pediatric polyclinic. Anti-HAV IgM and anti-HAV IgG serologic markers were determined using the ELISA method.

RESULTS: The mean age of 351 pediatric patients was 7.5 ± 4.2 ; of these, 198 (56.4%) were male and 153 (43.6%) were female. A total of 305 (86.9%) cases in this study were seronegative against hepatitis A. Anti-HAV IgG was positive among 46 (13.1%) patients, of these 22 (47.8%) were male and 24 (52.2%) were female. The mean age of seropositive cases was 8.4 ± 4.8 . Anti-HAV IgM seropositivity was not detected in this study.

CONCLUSION: The application of a routine hepatitis A vaccine among children will reduce the potential for the development of severe complications.

Key Words: Hepatitis A, seroprevalence, children, vaccination

Disseminate Pulmonary Hydatid Cyst Manifesting with Right-Side Cardiac Failure: Case Report

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OBJECTIVE: A case of disseminate pulmonary hydatid cyst (DPHC) manifesting with right-side cardiac failure was presented.

CASE: A 26-year-old man who presented with a cough, dyspnea, tachycardia, and chest pain was hospitalized with suspected pneumonia. The patient had a poor general condition and was conscious. On physical examination, fever: 37.3°C/axillary, blood pressure: 165/100 mmHg, cardiac pulse: 114/min, remarkable bilateral pretibial edema, peripheral cyanosis, and disseminated rales and rhonchi were found. On laboratory examination, leucocyte count: 4800/mm³ (68% granulocyte), hemoglobine: 12.0 g/dL, erythrocyte sedimentation rate: 43 mm/hour, and C-reactive protein: 8.8 mg/dL, IgE 1060 IU/mL, SaO₂ 81.8%, PaCO₂ 44.6 mmHg, were found. Chest radiography showed multiple disseminated cystic formations, and thorax computed tomography showed marked dilatation in the pulmonary artery, and multiple cystic formations in the lung area (Figure 1,2). Echocardiography revealed the following: a remarkable dilatation in the right atrium and ventricle, dilatation of the hepatic vein, and 3rd degree cardiac insufficiency. From the patient's detailed medical history, it was discovered that he had undergone a right-side cardiac operation six months previously because of right atrial hydatid cystic disease. A DPHC was considered due to the ruptured hydatid cyst during the cardiac operation on the patient. Thus, albendazole 800 mg/day was started and recovery was dramatic after this treatment.

CONCLUSION: This is the first case of DPHC disease presenting with right-side cardiac insufficiency. Severe complications may occur due to ruptured hydatid cyst when the maximum attention is not given to patients operated on for this condition.

Key Words: Hydatid cyst, cardiac failure, pulmonary diseases



Figure 1. Chest radiography.



Figure 2. Chest computed tomography.



The First Ulceroglandular Tularemia Case Occured After a Tick Bite in Turkey Where Oropharyngeal Tularemia is Prevalent

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Tularemia is a zoonotic infection and transmitted by inoculation, ingestion or inhalation of *Francisella tularensis*. Oro-farengeal form is the most common clinical aspect of the disease in Turkey. In this study, a new transmission route, a tick bite is described. It is showed that tularemia is not only food-borne but also a tick-borne disease in Turkey.

The case is a 58 years old woman from Aegean region of Turkey and engaged with a small ruminant livestock animal. She had a swollen and ulcerated lesion around to the tick's attachment site at occipital region and also had lymph-adenopathies at the right posterolateral region of the neck. Agglutination test for tularemia was positive with a titer value of 1/160. Bacterial DNA was detected in the lymphnode aspirate by TaqMan RT PCR in which ISFtu2 specific primers and probes were used. Streptomycin and doxycycline therapy was applied for treatment. After the specific diagnosis, an epidemiological investigation was performed in the area where the patient lived. No one was found to have similar symptoms in her family or village. History of tick bite, poor hygienic conditions of the patient's house, stall and haystack, using natural water without chlorination were recorded as environmental risk factors.

This patient identified for the first time in the Aegean region in Turkey is a typical case of ulceroglandular tularemia. No report in Turkey was encountered in the literature describing a tularemia case via vector as tick transmission. This was the first report causing a tick-borne tularemia in Turkey.

Key Words: Tularemia, ulceroglandular tularemia, tick-borne



Brucellosis: Report of 2 Cases

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Brucellosis is an infectious disease that can occur sporadically and in small outbreaks, and represents a significant public health problem. The clinical picture is diverse, ranging from asymptomatic forms, forms with less severe clinical picture and severe septic forms that can be fatal. The paper describes two cases.

CASE 1: Patient M.Z., born in 1968, with severe clinical manifestations of brucellosis and negative epidemiological data. Discharge diagnoses were: brucellosis, septicemia specificata alia, Embolio pulmonum massive, Sacroilitis sin. Etiological agent was confirmed by positive blood culture, positive serology and magnetic resonance imaging. Patient was treated for one year, after which the serological tests became negative.

CASE 2: R.M. infant, 10 months old, with moderate clinical picture and positive epidemiological diagnosis. Discharge diagnosis was brucellosis. Etiological agent was confirmed by positive serological tests. Treatment is in progress. Etiological treatment was done with antimicrobial drugs. Both patients were cured, and without complications so far.

CONCLUSION: Brucellosis requires a multidisciplinary approach based on various forms of the disease. Quick diagnosis reduces complications, and thus influences the outcome.

Key Words: Brucellosis, adults, children



Rapid Diagnosis of Central Nervous System Tuberculosis: A Case Report

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A 38 years old woman presented with atypical symptoms of tuberculous meningitis. The *Mycobacterium tuberculosis* was not detected initially in the cerebrospinal fluid (CSF) using the polymerase chain reaction. In spite of that anti-tuberculous treatment had been started. Diagnosis was confirmed later using BACTEC CSF culture system and CSF culturing on Lowenstein-Jensen medium. Central nervous system tuberculosis is the most serious form of tuberculosis and it often presents with nonspecific signs and symptoms. Early diagnosis and prompt treatment is important to minimise complications and reduce mortality. Delayed diagnosis can result in rapid progression of neurological deficits and poor prognosis. Polymerase chain reaction and other nucleic acid amplification methods are becoming increasingly useful for the rapid detection of *M. tuberculosis* in the CSF, although test is expensive and less sensitive than culture and there is the potential for false-negative results to occur in samples containing very few organisms (< 2 colony forming units/mL). As long as tuberculosis continues to flourish in developing countries tuberculous meningitis will remain constant threat, so high level of suspicion is essential.

Key Words: Tuberculous meningitis

Three Invasive Infections Caused by Oral Flora After Dental Manipulations: Case Report

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INTRODUCTION: Prophylactic antibiotics are not given in healthy individuals before dental procedures, but life-threatening infectious complications can develop. Here, three different invasive infections caused by dental flora after dental manipulation (acute bacterial meningitis, brain abscess and complicated deep neck infection) are reported.

CASE 1: Thirty five year-old diabetic female patient having five days of headache was admitted to the emergency unit with seizure. The stereotactic biopsy of the lesion (2.5 cm in diameter) in capsula interna (on cranial CT) was in consistent with brain abscess. *Streptococcus constellatus* and *Eikenella corrodens* grew in culture.

CASE 2: Fifty two year-old newly diagnosed diabetic male patient with fever, erythema, warmth and swelling of the neck and skin and soft tissue over sternum was admitted to our clinic. Cellulitis extended to his face and thorax. USG and CT of his neck showed abscess of the subcutaneous tissue. Staining of the pus revealed gram-positive cocci in chains but the culture remained sterile.

CASE 3: Fifty nine year-old female patient having Waldenström macroglobulinemia and splenectomy in her past medical history was admitted to the emergency unit with fever, nausea and vomiting. Although she had no signs of meningeal irritation, her CSF findings compatible with bacterial meningitis. Gram staining revealed abundant leucocytes and gram-positive cocci, *Streptococcus bovis* was isolated from CSF culture.

CONCLUSION: We think that, the requirement of antimicrobial prophylaxis before dental procedures should be re-evaluated for specific patient and age groups.

Key Words: Odontogenic infection, antimicrobial prophylaxis, meningitis, brain abscess, deep neck infection

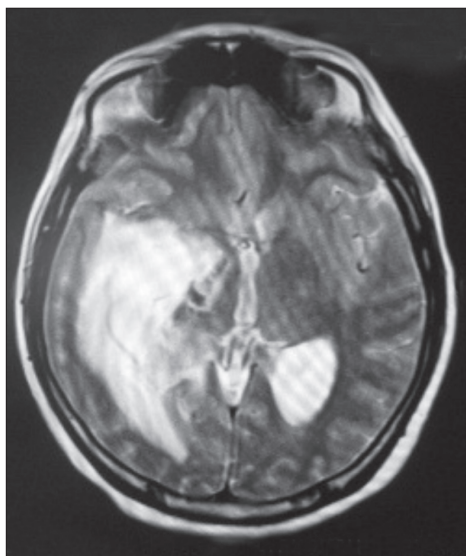


Figure 1. Cranial MR image of the 1st case: abscess near right occipital horn with heterogeneous contrast enhancement.



Figure 2. Cellulitis/deep neck infection extending to soft tissue over the sternum and abscess formation in the neck (2nd case).

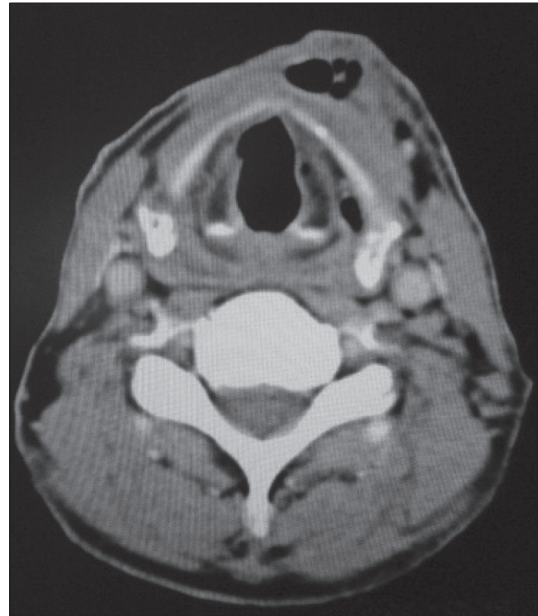


Figure 3. CT image of the neck (2nd case): Soft-tissue infection and abscess prominent on the mandibula level, involving the subcutaneous tissue.

Table 1. Clinical and laboratory characteristics of the patients

	Dental procedure	Predisposing condition	Infection site	Etiology	Initial treatment	Clinical outcome
1 st case	Dental prosthesis (15 days ago)	DM	Brain abscess	<i>S. constellatus</i> , <i>E. corrodens</i>	Ceftriaxone+ Metronidazole	Followed in ICU
2 nd case	Dental extraction (10 days ago)	DM	Deep neck and thoracic infection	Gram-positive cocci in chains, culture sterile	Ampicillin-Sulbactam	Cure
3 rd case	Dental filling (hemorrhagic) (7 days ago)	WM Splenectomy	Meningitis	<i>Streptococcus bovis</i>	Ceftriaxone	Cure

WM: Waldenström macroglobulinemia, DM: Diabetes mellitus.



Acute Generalized Exanthematous Pustulosis after Ceftriaxone Use Presented Like Sepsis: A Case Report

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Acute generalized exanthematous pustulosis (AGEP) is an uncommon disorder, characterized by the acute onset of multiple pruritic, small, non-follicular, sterile, superficial pustules between erythematous and edematous skin. It is frequently caused by medications, mainly antibiotics and particularly with beta-lactams. We report a case of ceftriaxone induced AGEP which presented like sepsis.

A 70-year old female patient was being followed under ceftriaxone treatment with the diagnosis of pyelonephritis. Under ceftriaxone her fever subsided, CRP level decreased and the general condition was improved within two days. However, at the third day of ceftriaxone, a sudden increase in fever (38.9°C) and confusion was observed. She became hypotensive, tachycardic and tachypneic. Simultaneously, erythematous pustular lesions were detected on the abdominal and dorsal skin areas rapidly extending to the lower extremities (Figure 1) and oral mucosa (Figure 2). Laboratory tests revealed leukocytes 34.660/mm³ with neutrophilia (94%) and eosinophilia (2.9%, 930/μL), CRP > 300 mg/dL. The treatment was switched to meropenem + teicoplanin because of the presumed diagnosis of sepsis. *Escherichia coli* was isolated in urinary culture pending antibiotic susceptibility. The lesions improved gradually within 48 hours and completely disappeared 10 days after discontinuing ceftriaxone. Definite diagnosis of AGEP was established with histopathological examination of skin biopsy and with a validation score of 10 over 10 point. As conclusion; AGEP is a rare case that was not well known in infectious disease practice, might resemble sepsis, usually associated with beta-lactams and this reaction might not be seen with another beta-lactam antibiotic.

Key Words: Ceftriaxone, rash, acute generalized exanthematous pustulosis, sepsis

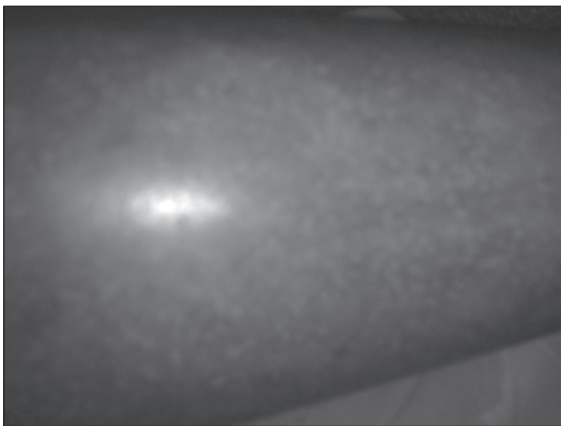


Figure 1.



Figure 2.



Antimicrobial Resistance of *Escherichia coli* as an Aetiological Factor of Urinary Tract Infections

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INTRODUCTION: The antimicrobial resistance of *E. coli* is different for the community-acquired and hospital-acquired clinical isolates.

AIM: To determine and compare the antimicrobial resistance of *E. coli* as an aetiological factor of hospital-treated, non-hospital treated, and hospital-acquired urinary tract infections.

METHODS: Antimicrobial resistance was determined by the disk diffusion method on Mueller-Hinton agar. The relation between the number of resistant isolates and the total number of tested isolates determined the percentage of the antimicrobial resistance. The antimicrobial resistance was compared by the T- test different of proportion.

RESULTS: The antimicrobial resistance of *E. coli* differs among the three groups of patients. The clinical isolates of hospital-acquired UTIs indicate a higher level of antimicrobial resistance to all antimicrobial medicines, and significantly higher level of resistance to aminopenicillins, cefuroxime, ceftriaxone, gentamicin, and cotrimoxazole.

Key Words: *E. coli*, antimicrobial resistance, urinary tract infections



Epidemiological and Clinical Manifestations of *Clostridium difficile*- Associated Diarrhea

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AIM: *Clostridium difficile* is the most common cause of intrahospital acquired infectious diarrhea in developed countries. The aim of this study is to analyze the clinical course and outcome in the two-year period in our clinic.

METHODS: This retrospective study included 52 patients who had more than three stools daily and a positive ELISA test *C. difficile* toxin.

RESULTS: The two-year period was confirmed *C. difficile* infection in 52 patients: Male 55%, > 65 years old 65%, with multiple comorbidity 78%.

CLINICAL INDICATORS: All surgical patients (70%) were receiving ciprofloxacin prophylaxis during 10 days. Most of the patients before hospitalization were repeated outpatient treated with antibiotics. Fever was present in 35% of patients, abdominal pain 51%, three or more watery stools per day 100%.

LABORATORY FINDINGS: Leukocytosis > 14 (27%), creatinine > 150 (23%), albumin < 25 (45%), potassium < 3 (23%), ELISA toxin in the stool test were positive in 100% of patients.

OUTCOMES: Recurrence 9%, complications 4%, lethal outcome 9%. Incidence in 2009.: 20/1000 release, in 2010. 15/1000 release, the difference was not statistically significant (p> 0.05).

CONCLUSION: *C. difficile* infection in our patients was associated with surgery and perioperative treatment with antibiotics of the quinolone group. Among our patients were mostly older people with multiple comorbidity. Severity of the disease and its outcome imposed by the need to change current policies and practices in the use of antibiotics.

Keywords: *Clostridium difficile*, infection, diarrhea, intrahospital



Deep Vein Thrombosis and Pulmonary Embolism After Varicella in a Case with Factor V Leiden Mutation and Activated Protein C Resistance

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We aimed to present the case upon detection of Factor V Leiden mutation and activated protein C resistance in a patient who developed deep vein thrombosis (DVT) and pulmonary embolism after varicella zoster virus (VZV) infection.

A 19-year old male patient presented with fever at the 10th day of VZV infection, and pruritic vesicopustular skin lesions. Leukocyte and CRP levels had increased. Acyclovir and ampicillin-sulbactam therapy were started. On the fourth day of hospitalization, left leg DVT and pulmonary embolism developed. Anticoagulant therapy was started. Laboratory tests revealed activated protein C resistance and Factor V Leiden mutation. Symptoms of the patient improved with anticoagulant treatment. Development of thrombosis during the course of VZV infection, is very rare. In thrombosis developed cases the causes that create thrombosis should be explored.

Key Words: Varicella, pulmonary embolism, Factor V leiden mutation

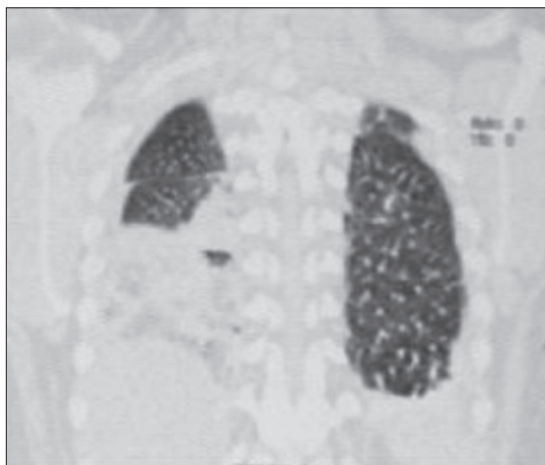


Figure 1. Image of thoracic angiography.

Weil's Disease with Prolonged Renal Failure and Marked Hyperbilirubinemia: Case Report

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INTRODUCTION: Acute renal failure in Leptospirosis can develop because of tubulointerstitial nephritis and acute tubular necrosis. Renal functions usually normalize with early antimicrobial and supportive therapy (hemodialysis). A patient presenting with acute renal failure and marked hyperbilirubinemia is reported here. The aim of this report of Weil's disease is to emphasize the importance of early hemodialysis with the possibility of prolonged renal failure despite full medical care.

CASE: A 50 year-old male building- worker presented with a week history of nausea, vomiting, abdominal pain, cough and jaundice. He had fever, tachycardia, conjunctival suffusion (Figure 1), diffuse petechial rash, icterus (Figure 2), crepitations on both lungs and hepatomegaly. He stated exposure to water contaminated with mice feces. Leptospirosis was considered as the possible diagnosis because of neutrophilic leukocytosis, thrombocytopenia, elevated bilirubin (Total bilirubin: 26 mg/dL, direct bilirubin: 23 mg/dL) and transaminase levels and acute renal failure. Initial ELISA test for Leptospiral IgM ve IgG were negative. Ceftriaxone 2 x 1 g IV was given and daily hemodialysis was performed. A week later, repeated ELISA test revealed five times increase in leptospiral IgG titer which confirmed our initial diagnosis. Antimicrobial therapy was given for two weeks but hemodialysis continued for 15 weeks.

DISCUSSION: Although renal functional recovery has commonly been reported to be fast and complete in Weil's disease, rarely renal failure may persist for a long time. We thought that tubulopathic effect of bilirubin could play a role in prolonged duration of renal failure in our patient because of marked hyperbilirubinemia.

Key Words: Weil's disease, leptospirosis, renal failure, hyperbilirubinemia, jaundice, hemodialysis, petechial rash



Figure 1. Conjunctival suffusion and icterus of Weil's disease (Written informed consent of the patient was obtained for publication of this picture).



Figure 2. Diffuse petechial rash all over the body and icterus of the skin (Written informed consent of the patient was obtained for publication of this picture).



Effect of Infantile Bacterial Meningitis on Incidence of Hyperactivity in School Children

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Bacterial meningitis in neonatal and infant periods causes numerous neurological and cognitive sequela depending on the cause and degree of the brain damage. Attention-Deficit Hyperactivity Disorder (ADHD) is a developmental disorder manifested in inattention, impulsiveness and hyperactivity. Objectives of this research work were the following: to identify incidence of hyperactivity in school children having suffered from bacterial meningitis during the first year of life; identify a correlation between the incidence of hyperactivity and gravity of the clinical picture in children who suffered from bacterial meningitis during the infant period.

The study included 60 respondents who suffered from bacterial meningitis during the first year of life and 60 school children of approximately the same age who have had no history of meningitis. The age of children in both the respondent and control groups was approximately the same (eight years).

The incidence of ADHD was considerably more common in the respondent group (62%) than in the control group of school children (5%). In both groups, the first symptoms of hyperactivity have manifested during the third year of life. 50% of respondents suffered from meningitis during the first month of life. Statistically, severity of the clinical picture of meningitis has a considerable correlation with the incidence of ADHD.

ADHD is more common in children who suffered from bacterial meningitis during the infant period compared to their age-mates who have not suffered from meningitis. There is a significant statistical correlation between an overall severity of the clinical picture of meningitis and incidence of ADHD.

Key Words: Bacterial meningitis, attention-deficit hyperactivity disorder, school children

Evaluation of Nosocomial Infections and Risk Factors in Critically Ill Patients: A Seven-Year Prospective Cohort Study

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Because of their many risk factors for nosocomial infections, intensive care units (ICUs) are high risk departments. The aim of this study, carried out prospectively between January 2004 and December 2010, was to determine the nosocomial infections, risk factors, and pathogens in ICU of a university hospital. A total of 697 infectious episodes (43.1 per 1000 patient days) were diagnosed in 408 out of 1112 patients. The most frequently observed infections were bloodstream infections (17.9 per 1000 patient days) and nosocomial pneumonia (14.9 per 1000 patient days). Of the primary bloodstream infections, 56.2% were associated with central venous catheters and 21.4% with arterial catheters; 93.4% of the nosocomial pneumonia were associated with ventilators and all the urinary tract infections with urinary catheters. The presence of central venous catheters was determined to increase the development of infection by 5.95 times ($p=0.000$), that of arterial catheters by 4.15 times ($p=0.0001$) and of ventilators by 4.35 times ($p=0.000$). High APACHE II scores, length of hospitalization and the length of use of invasive devices were determined to influence infection development ($p=0.000$). *P. aeruginosa*, *A. baumannii* and *S. aureus* were the commonest pathogens responsible for nosocomial infections. The rate of nosocomial infection in our hospital ICU is quite high. The most frequently observed nosocomial infections in the ICU are bloodstream infections and pneumonia, most of these infections being associated with the use of invasive devices.

Key Words: Nosocomial infections, intensive care units, bloodstream infections

Table 1. Risk factors affecting nosocomial infection development

Patient characteristics	Non-nosocomial		p	OR	95% CI
	Nosocomial infection (n= 408)	infection (n= 704)			
Age	49.2 ± 19.8	469 ± 21.6	0.103		
Gender (male)	255 (62.5%)	444 (63.1%)	0.850	0.98	0.75-1.27
APACHE II	19.0 ± 4.9	17.4 ± 5.6	0.000		
Length of hospitalization	26.0 ± 17.4	7.9 ± 11.1	0.000		
Invasive Interventions					
CVC	365 (39.5%)	414 (58.8%)	0.000	5.95	4.14-8.57
Mean CVC days	18.3 ± 13.3	4.4 ± 7.9	0.000		
AC	400 (98%)	650 (92.3)	0.0001	4.15	1.88-9.54
Mean AC days	23.1 ± 16.1	6.7 ± 9.6	0.000		
Ventilator	375 (91.9%)	309 (72.3%)	0.000	4.35	2.89-6.58
Mean ventilator days	18.5 ± 16.0	4.6 ± 8.1	0.000		
UC	406 (99.5%)	695 (98.7%)	0.345	2.63	0.53-17.69
Mean UC days	25.6 ± 17.0	7.7 ± 11.1	0.000		



A Case Report: Neurobrucellosis Mimicking Demyelinating Disease

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INTRODUCTION: Brucellosis is a common zoonotic infection in many parts of the world including the Mediterranean and Middle Eastern countries. Turkey is one of the endemic countries for brucellosis. Brucellosis is a multisystem disease that may present with a broad spectrum of clinical manifestations. Neurobrucellosis may develop at any stage of disease and may have widely variable manifestations.

CASE REPORT: A 45 year old woman presented with a six month history of difficulty in walking and weakness in her left arm. She had a history of treatment for brucellosis two years ago. Neurological examination showed spastic paraparesis and dysmetria in her left arm. She had demyelinating lesions on brain and thoracic magnetic resonance imaging (MRI). The investigation of cerebrospinal fluid (CSF) revealed 10 cells/mL (lymphocytes, 90%), a protein concentration of 78 mg/dL, a glucose level 48 mg/dL and the concurrent blood glucose level of 116 mg/dL. Serum and cerebrospinal fluid (CSF) was found as positive for brucella agglutination tests. The patient received treatment with ceftriaxone (2 g, bid, IV), rifampicin (600 mg/d, PO) and doxycycline (100 mg, bid, PO) for 3 weeks, then continued with rifampicin (600 mg/d) and doxycycline (100 mg, bid, PO). After six months of antibiotic treatment for neurobrucellosis, the patients clinical symptoms and thoracic demyelinating plaque resolved. But improvement was not achieved on brain demyelinating lesions.

CONCLUSION: In endemic regions, the patients with unexplained neurological symptoms should be considered for neurobrucellosis. Neurobrucellosis can be manifested like demyelinating diseases.

Key Words: Neurobrucellosis, demyelinating disease



Distribution of Yeasts Isolated from Vaginal Culture According to Age Groups

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AIM: Vaginal candidiasis is a frequently encountered condition. In the present study, our aim was to determine distribution of yeasts, which were grown in the culture of vaginal swab samples according to age groups.

MATERIALS and METHODS: Seven hundred and eighty three samples, which were referred to microbiology laboratory for culture between January 2008 and June 2010 were investigated retrospectively. Referred swabs were inoculated to blood agar and Sabouroud dextrose agar (Merck, Germany). Germ tube identification test and automated Vitek 2 Compact device (BioMérieux, France) were used for identification.

FINDINGS: Yeast growth was found in 147 (18.8%) of all samples. Mean age was 34.49 ± 9.70 years (range: 15-66 years) among patients with yeast growth. Growing yeasts were identified as follows: *Candida albicans* in 57 (38.77%), *Candida glabrata* in 28 (19.04%), *Candida krusei* in 10 (6.8%), *Candida kefir* in 7 (4.76%), *Candida tropicalis* in 2 (1.36%), *Candida parapsilosis* in 1 (0.68%) and non-albicans *Candida* spp. in 42 (28.57%) patients. Distribution of isolated yeasts according to age groups was shown in Table 1.

CONCLUSION: It was found that, among the isolated species, the most common agent that cause vaginal candidiasis was *C. albicans* in all age groups. It was seen that *C. glabrata* was the second most common agent.

Key Words: Vaginal culture, yeasts

Table 1. Distribution of isolated yeasts according to age groups

Yeasts	Age groups			Total	
	15-34	35-49	≥ 50	n	%
<i>Candida albicans</i>	30	25	2	57	38.77
Non-albicans <i>Candida</i> spp.	18	24	-	41	28.57
<i>Candida glabrata</i>	12	14	2	28	19.04
<i>Candida krusei</i>	4	5	1	10	6.80
<i>Candida kefir</i>	3	3	1	7	4.76
<i>Candida tropicalis</i>	-	2	-	2	1.36
<i>Candida parapsilosis</i>	-	1	-	1	0.68
Total	67	74	6	147	100



A Case of Acute Hemorrhagic Cystitis Caused by *Salmonella paratyphi A* in a Pediatric Patient

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INTRODUCTION: Urinary tract infection (UTI) caused by *Salmonella* spp. is known rare even where organisms are endemic.

CASE: Seven-year old boy admitted to emergency service with lower abdominal pain, dysuria, nausea and fever despite of receiving six days cefoxitin treatment. The patient was diagnosed as hemorrhagic cystitis. At the admission had fever (38.1°C) and suprapubic tenderness. In the laboratory hematuria (++++), leukocyte esterase (+++), Hb: 12.9 g/dL, RBC: 4.8 million/mm³, WBC: 11.800/mm³, PLT: 275.000/mm³, RDW-CV: 15.3%, sedimentation: 27 mm/hour; CRP: 30.2 mg/L and PTO (+), PTH (+) were found. *Salmonella paratyphi A* isolated from urine of culture in the third hospitalization day. Urine culture showed pure growth (> 10⁵ CFU/mL) of colonies were identified by conventional methods and repeated by automated system. Also, identification of this isolate confirmed by using *Salmonella* polyvalent antisera and identified as *S. paratyphi A* which was sensitive to ceftriaxone. A bacterium wasn't isolated from stool and blood. The patient treated with ceftriaxon for 7 days. Control culture of urine sample was negative and patient had a full recovery.

CONCLUSION: We conclude that in case of acute hemorrhagic cystitis, *S. paratyphi* should be considered as causative agent in endemic area.

Key Words: Urinary tract infection, *Salmonella paratyphi A*, hemorrhagic cystitis



Investigation of Febrile Neutropenia Attacks and Risk Factors in Cancer Patients

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Febrile neutropenia is the most important factor responsible for the morbidity and mortality in cancer patients. In this study, febrile neutropenic attacks seen on 100 patients who are consulted between January 2008 and December 2009 were prospectively evaluated. Only first attack of each patient included in the study.

Fifty eight of patients were female and 42 were male. Mean age of patients was 59.4 ± 13.4 (24-90). Primary malignancies were hematologic malignancy in thirty patients and solid tumors in seventy patients. According to MASCC criteria twenty nine of patients were in low risk group whereas seventy one patients were in high risk group. Mean absolute neutrophil count, mean duration of neutropenia period and mean duration of hospitalization time were 247.8 ± 25.2/mm³, 3.31 ± 1.86 d, 4.37±0.69 d, respectively. Of the 100 neutropenic attacks; twenty two were clinically defined infection, thirty nine were microbiologically defined infection and thirty nine were fever of unknown origin. Most frequent infection sites were pneumonia and pyelonephritis due to clinical and microbiological findings. Isolated strains included 44 gram-negative bacillus, 4 gram-positive coccus and 9 *Candida* spp. *Escherichia coli* was the most frequent isolated agent in these strains (n= 27, 47.3%). Empirical treatment of patients included monotherapy (61%) and combined therapy (39%). Most frequently used antimicrobial agents in monotherapy were cefoperazone-sulbactam. Mean fever response period was 2.6 ± 0.16 day. Fifteen of patients were died in the febrile neutropenia attack.

Key Words: Febrile neutropenia, cancer, infection



Does Treatment Effect the Levels of Serum IL-6, IL-8 and Procalcitonin in Diabetic Foot Infection? A Pilot Study

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INTRODUCTION: We aimed to investigate about serum PCT; IL-6 and IL-8 levels and how they are affected by the treatment.

MATERIALS and METHODS: Fifty diabetic patients with infected foot ulcer were included to the study. The demographical information, diabetes background, anamnesis of their foot ulcers and given therapies of the participants were received at the first visit. 8-10 hours' fasting blood samples were taken before the treatment to study blood count, routine biochemical parameters, HbA1c, ESR and CRP as well as IL-6, IL-8 and PCT. The same parameters were studied from the repeating samples of under cure patients at the 14th day.

RESULTS: The pretreatment results of the 50 patients showed positive correlations between PCT and either ESH ($r=0.49$, $p<0.001$), or CRP ($r=0.56$, $p<0.001$). Similarly, there was a positive correlation between IL-6 and ESH ($r=0.46$, $p=0.001$), just like as it was between IL-6 and CRP ($r=0.54$, $p<0.001$).

When the patients were grouped at 14. day and analysed again, the levels of ESR, CRP and PCT (0.6 ± 2.1 and 0.05 ± 0.02 , $p=0.007$, respectively) were significantly decreased while IL-6 was decreased at close range to statistical significance at healing patients (97.5 ± 147.2 and 47.1 ± 77.6 respectively; $p=0.05$), but they did not at nonhealing patients. Anyhow IL-8 levels were not changed significantly.

DISCUSSION: PCT and IL-6 may be useful like CRP and ESR in diagnosis and follow up of diabetic foot infection, but IL-8 not. Further investigation is needed.

Key Words: IL-6, IL-8, procalcitonin, diabetic foot ulcer



Tularemia Outbreak in Afyonkarahisar, Turkey

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Tularemia is a bacterial zoonosis rodents, rabbits and hares caused by gram-negative, facultative intracellular bacteria of the species *Francisella tularensis*. Oropharyngeal form is the most frequently reported form of the disease from Turkey. In 2010 and 2011 the outbreaks of tularemia, the first of tularemia cases in our region. The aim of this study was to the clinical and laboratory findings tularemia patients.

In 2010 and 2011, two tularemia outbreaks occurred in Afyonkarahisar. During tularemia outbreaks in the Afyonkarahisar region of Turkey, total of 67 patients were diagnosed and evaluated. Serum and tissue samples were sent to Refik Saydam National Public Health Agency in order to test for tularemia, microagglutination test (MAT) and polymerase chain reaction (PCR). All the cases were diagnosed on clinical, bacteriological and serological methods. Oropharyngeal, glandular and ulceroglandular forms of the disease were detected. The majority of the patients presented with oropharyngeal tularemia (97%). The most common symptoms were fever (85.1%), malaise (77.6%) and sore throat (71.6%). The patients were treated with gentamicin (82.1%) or ciprofloxacin (17.9%). As a result, tularemia should be considered in patients with cervical lymphadenopathy and sore throat in endemic region.

Key Words: Outbreak, treatment, tularemia

Varicella Pneumonia in an Hepatitis B Virus Carrying Adult Patient: A Case Report

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Varicella-zoster virus (VZV) pneumonia, although rare, is the most serious complication that commonly affects adults with high mortality rates. In this study, we describe a case of VZV pneumonia of a 29 years old male patient who was hepatitis B virus carrier. The patient presented with a 5-days history of fatigue, sore throat, fever, cough and mild dyspnea. He had an exanthematous vesicular rash that had started one day later the sore throat began. Initially, he had recieved cefuroxime during 6 days before administration to our hospital but didn't recovered from fever. The rash had spreaded to all body including hairy skin. He hadn't have history of varicella nor did he had been vaccinated against it. On physical examination the patient, who was pale but not joundiced was not febrile (37.0°C) and had normal vital signs when administered. Examination of the respiratory system was normal. Skin examination exhibited lots of polymorphic rash with papul/vesicles, pustules, and crusty lesions in whole body. Laboratory findings was; Hb: 16.6 g/dL, RBC: 5.6 million/mm³, WBC: 4200/mm³, PLT: 275.000/mm³, sedimentation 17 mm/h, CRP 1.7 mg/L, AST 74, ALT 145, VZV IgM (+) and IgG (+), HBsAg (+), HBV-DNA (-), anti-HIV_{1/2} (-). Serum urea, creatinine, bilirubines, electrolytes were normal. Chest radiography showed pneumonic infiltration in middle zone of lungs. The diagnosis of varicella pneumonia was made on the basis of the rash, radiography and VZV antibody. The patient was treated with valacyclovir and clarithromycin without discrimination of primary and secondary pneumonia. Skin lesions disappeared after ten days and the patient had a full recovery.

Key Words: Adult pneumonia, varicella-zoster virus, hepatitis B



Figure 1. Polymorphic rash with papul, vesicles, pustules, and crusty lesions on the patients neck.



Figure 2. Nodular infiltrations in middle zone of lungs.

An Unusual Case of Endocarditis: Isolated Pulmonary Valve Endocarditis in Patient with Patent Ductus Arteriosus

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BACKGROUND: Right-sided endocarditis is uncommon, comprising only 5-10% of all cases of infective endocarditis. The majority of cases involve the tricuspid valve. Pulmonary valve endocarditis is a rare disease, usually associated with congenital heart disease and especially with patent ductus arteriosus (PDA). It accounts for 1.5 to 2.0% of all endocarditis.(2). A case of pulmonary valve endocarditis in a patient with patent ductus arteriosus is reported.

CASE: A 9-year-old woman was admitted to our hospital for a three-day history of high grade fever and recent development of chills, chest pain, cough and shortness of breath. On admission, the patient had a fever of 38.3 °C, elevated white cell count of 12.400/mm³, erythrocyte sedimentation rate (ESR) of 140 mm/h, CRP level of 123 mg/dL. Physical examination was significant for a hyperdynamic precordium, a continuous "machinery" murmur above the pulmonic region consistent with a patent ductus arteriosus, hepatomegaly, splenomegaly. Echocardiography showed a large echodense and very mobile multiple vegetations were on the pulmonary valve and hyperechogenic vegetations attached to the wall of the pulmonary artery (Figure 1). She was admitted in intensive care unit and was started on intravenous vancomycin and gentamicin as empirically for infective. The patient was subsequently treated for infective endocarditis with vancomycin and gentamycin for 28 days. Control echocardiography no vegetation on pulmonary valve and main pulmonary artery was seen.

CONCLUSION: Careful evaluation of pulmonic valve in echocardiography should be done, when ever vegetation is not detected in other valves, and clinical suspicion for infective endocarditis is high.

Key Words: Infective endocarditis, pulmonic valve, vegetation, patent ductus arteriosus

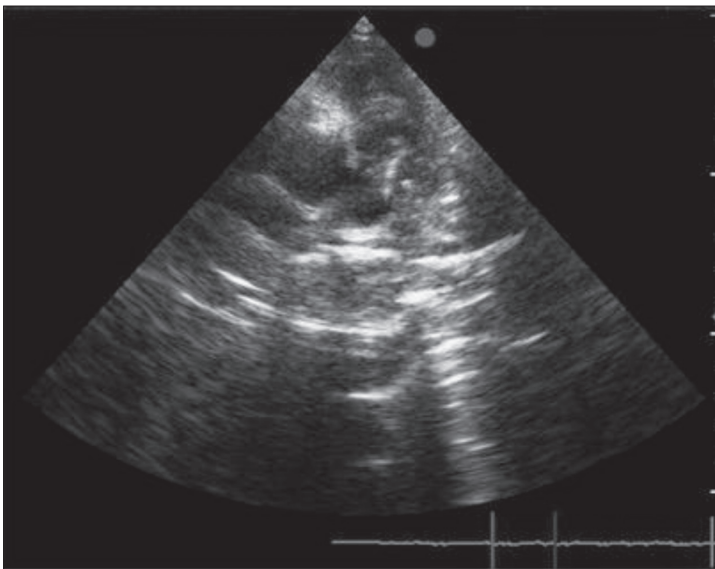


Figure 1. TTE showed a large echodense and very mobile multiple vegetations were on the pulmonary valve and hyperechogenic vegetations attached to the wall of the pulmonary artery.

A Case of Brusellar Spondylodiscitis Involving the Cervical Spine

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AIM: Brusellosis is a zoonotic infection transmitted from animals to humans especially whom consume unpasteurized milk products. Brusella lesions of the spine can occur at any level, but cervical involvement is rare. We report a rare case of brusellar spondylodiscitis, involving the cervical C6-C7.

CASE: A 53-year-old woman presented with a 1 week history of acute neck, left arm pain associated with decreased range of motion. She complained of fatigue, headache, weight loss, night sweats, fever for the past 3 months. White blood cell count (7400mm³), hemoglobin (12 g/dL) with in normal limits. Erythrocyte sedimentation rate (72 mm/h) and CRP (10.89 mg/dL) were high. Leukocyte formula revealed 27% lymphocytes, 59% neutrophils and 12% monocytes. Blood chemistry was within normal range. She was operated by ortopedics clinic and cervical vertebra corpectomy and debridement of the paravertebral granulomatous tissue deposits were performed followed by stabilization with anterior plating and bone grafting. Preoperative MR imagings of the patient show spondylodiscitis (Figure 1). Wright agglutination test for brucella was positive at 1/160 and Rose Bengal test was positive. She was treated with rifampin (600 mg/day orally) and doxycycline (200 mg/day orally). The patient's condition improved at 2 weeks after initiation of therapy. The therapy was stopped after 6 months.

CONCLUSION: Brusellosis should be considered in differantial diagnosis of the cervical spondylodiscitis in patients who reside in countries where the zoonosis is still endemic.

Key Words: Brucella, cervical spondylodiscitis

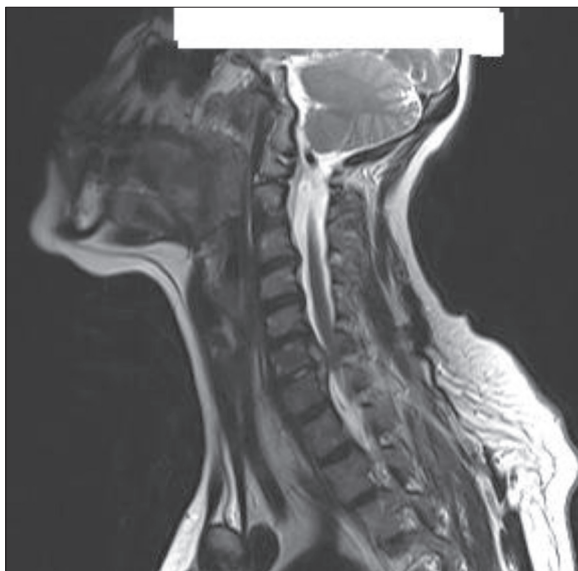


Figure 1. Preoperative MR imagings of the patient show spondylodiscitis.



An Unusual Case: Intramedullary Tuberculoma with Intravertebral Abscess

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AIM: Tuberculosis is still an important pathological entity in developed and developing countries. Of the patients with tuberculosis, 0.5-2% of patients develop tuberculosis of central nervous system. We report a very rare case of intramedullary tuberculoma with intravertebral abscess.

CASE: A 36 year-old male patient was admitted to our clinic with back pain, leg pain and progressive complain of weakness in both lower extremities. On neurological examination, there was 2/5 muscle strength on the right lower extremity whereas 1/5 on the left. The Babinski reflex was positive bilaterally and deep tendon reflexes were hyperactive. The patient was diagnosed as pulmonary tuberculosis and tuberculosis meningitis a year ago and was treated with 4 drug anti-tuberculosis regimen for one year. The laboratory examination revealed nonspecific findings. On thoracal MRI, T2 weighted sagittal images revealed diffuse thickening and irregularity in spinal cord and heterogenous increase in signal intensity. There was a nodular lesion intramedullary located at the level of T10, hypointense in T2 weighted images, which also showed contrast enhancement. Furthermore, intravertebral abscess with a peripheral contrast enhancement was shown in T11 and T12 vertebral bodies. On cranial MRI, T2 weighted axial images demonstrated hypointense nodular lesion in right temporal lobe. The patient diagnosed as intramedullary tuberculosis and anti-tuberculosis treatment was persisted and rehabilitation programme started. After 18 months treatment, patient's complains disappeared.

CONCLUSION: Tuberculoma should be considered in the differential diagnosis of all intramedullary space occupying lesions presence of extracranial focus of tuberculosis in countries endemic to tuberculosis.

Key Words: Intramedullary tuberculoma, tuberculosis, treatment



Serotype Distribution and Antimicrobial Susceptibility of *Streptococcus pneumoniae* Isolated from the Children with Pneumococcal Infections in Turkey

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The aim of this study was to determine the serotype distribution and antimicrobial susceptibility of *Streptococcus pneumoniae* strains isolated from invasive infections among children younger than five years of age in Turkey after routine vaccination with seven-valent conjugated pneumococcal vaccine (PCV-7).

In the scope of this multi-center study, a total of 287 clinical samples or strains isolated from the invasive infections were examined in our laboratory from May 2009 to December 2010. Isolates were serotyped by quellung reaction with the antisera panel and sequential multiplex PCR. Susceptibilities to penicillin, cephalexin, meropenem and vancomycin of the isolates were determined by E-test (AB Biodisk, Solna, Sweden).

A total of 60 pneumococcal strains were recovered from the all study group. The most frequent serotypes were 19F (20%), 3 (8.3%), 14 (6.7%) and 1 (6.7%). Serotype/serogroup 19F (20% of the strains), Pool I (8.6%), 6A (8.6%), 18C (5.7%), 9L/N (5.7%), 5 (5.7%), 3 (5.7%), 1 (5.7%) were the most common types observed among children \leq 5 years old. Vaccine serotype coverages were 34.4%, 48.7%, 65.9% for PCV-7, 10- and 13-valent pneumococcal conjugate vaccines, respectively. Twenty two strains (68.75%) were susceptible to penicillin, 7 (21.87%) were intermediate and 3 (6.25%) were resistant. All strains were susceptible to cephalexin, meropenem and vancomycin except one isolate.

We have gained some insight on the serotypes and susceptibility of invasive *S. pneumoniae* strains in Turkey following to PCV-7 vaccination. We consider that this multi-center study is a good background for monitoring the epidemiology of invasive pneumococcal diseases in Turkey.

Key Words: *Streptococcus pneumoniae*, serotypes, penicillin resistance



Liver Abscess Associated with the Oral Flora Bacteria *Streptococcus anginosus*

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INTRODUCTION: The low-virulence viridans streptococcus, a bacteria of the oral flora, rarely causes liver abscess. There is little published literature about the hepatic abscess associated with dental problems or dental treatments. A non-immunodeficient case of liver abscess associated with the oral flora bacteria *Streptococcus anginosus* is presented here.

CASE: A 40-year-old male patient was admitted to the hospital complaining of high fever and general malaise. A physical examination revealed poor oral hygiene; there were caries on many teeth, and he had hepatomegaly. A hepatic abscess was identified in his abdominal tomography. *S. anginosus* was isolated from the drainage material, and the bile ducts were normal in his MRI cholangiography.

CONCLUSION: Tooth disease and tooth treatments rarely cause hepatic abscess. It should be remembered that the oral flora bacteria *S. anginosus-mitis* group may cause transient bacteremia and lead to deep organ abscess in patients with poor oral hygiene; the agents against *S. anginosus* should be used for empirical therapy of the pyogenic hepatic abscess developed in these cases.

Key Words: Liver abscess, *Streptococcus anginosus*, oral flora, bacteremia



Spread of OXA-48-Positive *Klebsiella oxytoca* Isolates in Istanbul, Turkey

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The spread of carbapenemase-producing *Enterobacteriaceae* isolates is a significant threat to the management of nosocomial infections. In this study five OXA-48 producing *K. oxytoca* strains were analyzed.

The strains were isolated in April-July 2010. Two strains were isolated from same patient after three month interval. The antibiotic susceptibility tests were performed using the disc diffusion method and VITEK 2 system. Carbapenemase activity was demonstrated by the Modify Hodge Test. Beta-lactamase genes were detected by PCR and blaOXA-48 were sequenced. Genetic relatedness between *K. oxytoca* isolates were investigated by PFGE.

In general, the minimal inhibitory concentration (MIC) for imipenem, meropenem and ertapenem increased (Ertapenem: 2-4 µg/mL, imipenem: 4-8 µg/mL, meropenem: 0.25-1 µg/mL), however only one *K. oxytoca* isolate was resistant to meropenem (MIC ≥ 16) and ertapenem (MIC ≥ 8). blaOXA-48 genes in these isolates were demonstrated by PCR and sequence analysis. Additionally, four isolates co-produced at least two beta-lactamase from TEM, SHV, CTX-M or VEB-1 type. PFGE revealed three distinct profiles. Three strains which two of them were isolated from same patient hospitalized in pediatric intensive care unit were clonally related.

The identification of *K. oxytoca* isolates harboring blaOXA-48 but also ESBLs such as TEM, SHV, CTX-M, now VEB-1 type is a serious concern for carbapenems which are mostly a last resort for ESBL producing strains. The detection of OXA-48 producing strains in clinical laboratory may be difficult due to find susceptible range to carbapenems according to CLSI breakpoints. The dissemination of blaOXA-48 gene is not spread by a single *K. oxytoca* clone, several OXA-48-producing clones were distributed in Istanbul.

Key Words: Carbapenemase, OXA-48, ESBL



Brucellosis in Southeastern Anatolia of Turkey: A Retrospective Evaluation of 109 Cases

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AIM: The aim of this study was to evaluate the clinical, laboratory findings and therapeutic features of the patients inhabiting in Mardin province, in Southeastern Anatolia of Turkey.

METHOD: In this study, 109 patients with brucellosis, followed in departments of infectious diseases and clinical microbiology between June 2007 and July 2009 were evaluated retrospectively.

RESULTS: Fifty six (51%) of the patients were male and 53 (49%) were female. Mean age was 32.5 ± 17.6 (range 7-78) years. The patients were categorized as acute (75%), subacute (19%) and chronic (6%) brucellosis. Major transmission route was the consumption of unpasteurized fresh cheese. The transport of animals in the region are not controlled. Malaise, fever, myalgia arthralgia and sweating were the most frequently observed symptoms. The most common signs were fever 90.8%, arthritis 54.1%, splenomegaly 18.3% and hepatomegaly 11%. In view of laboratory findings, increased erythrocyte sedimentation rate was detected 43 mm/hour (39.4%), C-reactive protein 80 mg/dL (60%), serum transaminase levels 47 IU/L (43.1%) of the patients. Diagnosis was made based on the clinical features and positive Rose-Bengal test combination with an initial *Brucella* antibody titre greater than or equal to 160. The most frequently preferred antimicrobial regimen was rifampin and doxycycline combination.

CONCLUSION: The clinical presentation of the disease may show regional variations, it should be considered in the differential diagnosis of numerous diseases.

Key Words: Brusellosis, evaluation, Southeastern Anatolia of Turkey



A Case of Chest Wall Tuberculous Abscess

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AIM: Tuberculous abscess of the chest wall is rare and may mimic pyogenic abscess or tumor. The diagnosis may be difficult. We report a case of chest wall tuberculous abscess without pulmonary involvement.

CASE: A 34 year-old woman presented with a 1 month history of enlarging chest wall mass. She was also complaining of fatigue and back pain for the past 3 months. White blood cell count 5600 mm^3 , leukocyte formula with in normal limits. Erythrocyte sedimentation rate 56 mm/h and CRP 4.6 mg/dL were high. She has not history of tuberculosis and has normal immun status. Computerized tomography of thorax showed posterior chest wall abscess without evidence of underlying lung disease. Contrast enhanced MR image shows abscess formation with enhancing wall. Drainage of the abscess was performed, purulan material was obtained. PCR test was positive for *Mycobacterium tuberculosis* and by the 2. week there was a growth of basilli in Lowenstein-Jensen culture media. She received 12 months of antituberculous therapy with initial 4 drug regimen for 4 for months followed by two drugs.

CONCLUSION: Tuberculosis remains a major health problem in developing countries. Optimal treatment methods of chest wall tuberculosis with or without surgery are controversial. In endemic areas, tuberculosis must be in mind in patients presenting with a chest wall mass.

Key Words: Tuberculosis, chest wall, abscess



The Most Important Reason for Delay in Pediatric Surgery Operations: Upper Respiratory Tract Infection

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BACKGROUND: The most important disease causing delay in operation realisation in all children surgery clinics is upper respiratory tract infection (URTI). In this study, we aimed at pointing out the reasons for elective surgical intervention delays and the financial expenses that they cause, and providing our solution proposals.

MATERIALS and METHODS: Between January 2004 and December 2005, 150 cases included in our study (for 100 cases; their operation was cancelled in operation day because of their problems recognized preoperatively; for 50 cases those underwent surgery in their operation day). All cases have been chosen from patients pool that include patients need for elective surgery and having pathology for surgery in two years, randomly. These 50 cases used for control group.

RESULTS: Most frequently cause leading to delay operation was upper tract infection (90%). For the remaining patients, 7 cases were not operated on the date day because of anaemia, 2 cases because of viral pneumonia, and 1 case because of electrolyte imbalance. The mean hospital charges calculated was 81.31 \$ for the work group, and 28.44 \$ for the control group. In cost analysis, differences have been between groups statistically important ($p < 0.05$).

CONCLUSION: Because of these causes, upper and lower tract infections recognized in patient who will undergo surgery make operation delay essentially.

Key Words: Upper respiratory tract infection, elective surgery, cost, delaying operation



Left Retroperitoneal Hydatid Disease and Transthoracic Surgical Approach

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OBJECTIVE: This paper gives an overview of the literature between 2000 and 2010 on primary retroperitoneal hydatid cyst. There were only 13 left retroperitoneal hydatid cysts in the English literature. We reported one case of primary left retroperitoneal hydatid cyst with concomitant left diaphragmatic hydatid cyst.

CASE: A-21-year-old female admitted with abdominal pain. There was no abnormality in the laboratory tests. Thora-coabdominal computed tomography showed left intrapulmonary and left retroperitoneal round, cyst shaped masses. Suspected diagnosis was hydatid cysts. *E. granulosus* IgG was positive at 1/640 in the IFA test. Treatment with albendazole 15 mg/kg/day (4 weeks treatment, 2 weeks nontreatment periods). Follow up computed tomography showed decreased diameters of the cysts. Cystectomy planned for thoracic cyst. Left thoracotomy was applied and cystectomy was applied for diaphragmatic cyst. Phrenotomy and drainage of retroperitoneal cyst and capitonage applied via transthoracic approach. Patient was discharged home at the 5th day of postoperative period with treatment of albendazole. 6th month's follow up computed tomography showed no recurrence of cysts.

CONCLUSION: If a cystic lesion is determined in the retroperitoneal area in a patient living in an area of endemic hydatid disease, a differential diagnosis of hydatid cyst should be considered. Clinical, radiologic, serologic, and histopathologic evaluations should be made for a differential diagnosis.

Key Words: Hydatid cyst, albendazole, retroperitoneal area



Twenty Five Years with HIV/AIDS in the Lowest Prevalence Region: Epidemiologic and Clinical Profile

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OBJECTIVE: Turkey at present that have lowest HIV/AIDS prevalence is a country. We aimed to present the clinical and demographic profile of HIV/AIDS patients and to discuss the epidemiologic results.

METHODS: The retrospective study period was including between 1985-2010. We defined HIV/AIDS cases according to UNAIDS/WHO definitions. Epidemiologic data were obtained HIV/AIDS follow-up forms.

RESULTS: Total 201 patients were followed. Male/female ratio was 3.4 and mean age was 37.8. The most common way of transmission for all patients were heterosexual intercourse (63.6%), injected drug use (IDU) (13.4%), and homosexual intercourse (MSM) (15.38%). Twelve males were university graduates, 8 males were doing clerical job. The most common profession was truck drivers. All female patients were housewives except two unqualified workers. Weight loss, fever, weakness and dysphagia were the most common complaints at diagnosis. The most common opportunistic infection was candidiasis (42%) and tuberculosis (22.4%). At the first diagnosis the mean CD4 count of the patients was 169 mm³ (7-677). Fifty percent of patients consulted in stage-3. The main causes of death were wasting syndrom and tuberculosis. While the risk factors for HIV/AIDS were lower education level, unregistered sex workers, migration, unprotected sexual intercourse and young population; the factors on low prevalence were traditional circumcision of men, lower IDU and MSM than other country.

CONCLUSION: Although HIV/AIDS prevalence was lowest in Turkey; there is vulnerable population to HIV. For keeping of the low ratio the number of HIV testing should be increased especially in people at high risk of becoming infected.

Key Words: HIV, AIDS, epidemiology, diagnosis



Cases of Human Brucellosis in Tuzla Canton During Period 2005-2010

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INTRODUCTION: Brucellosis a disease also known as undulant fever, Mediterranean fever, Malta fever is a zoonosis and it is almost invariably transmitted by direct or indirect contact with infected animals or their products

GOALS: The goals of this research work is to show incidence of human brucellosis in Tuzla Canton, age and sex distribution, presumptive ways of infection, seasonal distribution, risk factors.

MATERIALS and METHODS: The retrospective analysis of the cases of human brucellosis in Tuzla Canton during period 01.01.2005-15.09.2010.

RESULTS: During period 01.01.2005-15.09.2010 in Tuzla Canton were reported 181 cases of human brucellosis, among them 86.74% were hospitalized, 13.26% were not hospitalized. Incidence of human brucellosis was the highest in 2008 (17.88), the lowest in 2005 (0.80). 79.01% of infected were men, 20.99% were women. Most of cases were in age group 25-49 years (51.93%). Most of cases reported in April (24.86%). The most presumptive way of infection was contact with animals (59.67%)

CONCLUSION: Brucellosis is a serious public health problem because of insidious course of illness, prolonged treatment, many of complications, work absence, economical aspects and is more serious problem in rural regions because of cultural customs and lack of education, hygiene procedures, health services. In rural regions children are in at high risk of infection because of their close contacts with animals, especially with newborn ones. Adults in a such regions usually have some kind of immunity or have symptoms and signs of chronic brucellosis.

Key Words: Human brucellosis, Bosnia and Herzegovina, Tuzla Canton, retrospective analysis

Table 1. Age distribution of human brucellosis in Tuzla Canton

Age group	Percentage of cases
0-6	1.66%
7-14	3.31%
15-24	10.50%
25-49	51.93%
50-64	25.97%
65+	6.63%

Table 2. Incidence of human brucellosis in Tuzla Canton

Year	Incidence (cases/100.000 inhabitants)
2005	0.80
2006	1.41
2007	2.62
2008	17.88
2009	7.62
2010	6.01

Table 3. Presumptive ways of infection with *Brucella* spp.

Contact with animals	Ingestion of animal products	No data
59.67%	8.84%	31.49%

Table 4. Seasonal distribution of human brucellosis in Tuzla Canton

Month	Percentage of cases
January	2.21%
February	4.97%
March	11.60%
April	24.86%
May	14.92%
June	11.60%
July	8.84%
August	3.87%
September	6.08%
October	3.87%
November	0.55%
December	1.10%
No data	5.52%

Table 5. Sex distribution of human brucellosis in Tuzla Canton

Men	Women
79.01%	20.99%



Epidemiological and Clinical Characteristics of Tularemia and the Effectiveness of Medical Treatments

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BACKGROUND: Tularemia is a zoonotic infection disease caused by *Francisella tularensis* and that generally appears in sporadic cases or occasionally in minor epidemics. It was widely observed in the Marmara and Western Black Sea regions in Turkey before 2005, and the number of cases in our region increased in 2009-2010. Clinically, it resembles many other diseases, for which reason incorrect treatments may be applied.

This study was intended to determine the epidemiological and clinical characteristics of patients monitored with a diagnosis of tularemia and the effectiveness of the treatments administered.

METHOD: Patients attending our hospital between January 2009 and March 2011 and diagnosed with tularemia were evaluated retrospectively. Patients' epidemiological and clinical characteristics, the treatments administered and post-treatment findings were recorded on patient monitoring forms. Data were transferred to SPSS and analyzed statistically.

FINDINGS: Of the 31 patients in the study, 61.3% were female and 38.7% male. At anamnesis, 29% used water from wells and 71% water from the network supply, 48.4% had a history of contact with animals and 87.1% a history of lethargy. At physical examination, 96.8% had a mass in the neck and 90.3% had fever. Gentamycin + doxycycline therapy was administered to 45.2% of patients, while levofloxacin, gentamycin and streptomycin were used for the other patients. After treatment, neck masses persisted in 48.4% of patients and complaints of lethargy and fever in 6.5%. Treatment of these patients was initiated once tularemia had been diagnosed (since the test results were announced some 3 weeks later). Lymphadenopathy excision was performed on 19.4% of patients in whom neck mass persisted.

CONCLUSION: Appropriate empiric antibiotherapy should be commenced without waiting for *F. tularensis* results in patients presenting with neck mass, fever and lethargy in regions with tularemia epidemics.

Key Words: *Francisella tularensis*, tularemia, epidemic



A Case of Brucellosis Presented with Acute Hepatitis and Bisitopenia

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Nineteen years old, male patient. Ten days earlier, he applied to our clinic with the following complaints; fever, sweating, low back and leg pain, lassitude, lack of appetite, nausea and vomiting. Vital signs were 40.3 °C of temperature, In physical examination, he was bad and exhausted in general appearance with icteric skin and scleras and his right hypochondriac region was tender. Laboratory studies showed a mild leukopenia of 3500/ μ L, with a trombosit of 89.000/ μ L. Biochemical examinations revealed following.

RESULTS: AST, 771 U/L; ALT, 471 U/L; total bilirubin, 2.61 mg/dL; direct bilirubin: 1.45 mg/dL and albumin, 3.7 g/dL. HB-sAg, anti-HBc total, anti-HBc IgM, anti-HAV IgM, and anti-HCV were found as negative. In upper abdominal ultrasonography, liver size was minimally increased (160 mm), and its parenchymal echogenicity was diffusely decreased. The wall of gall bladder was diffusely increased and spleen became larger (179 x 69 mm). At the day of 2, the result of standardized brucella tube agglutination was positive with a 1/160 titer. A treatment of streptomycine of 1 g per day intramuscularly and tetracycline of 2 g per day orally was started. At the day 5 of his admission, the fever was controlled and symptoms were relieved. General condition was improved. He was followed up for two weeks. At discharge, his symptoms and findings excluding lassitude were totally improved. liver function tests improved at the day of 28. Streptomycine and tetracycline were ended at the day of 21 and 45, respectively. After one year of follow-up, no relapse was observed.

Key Words: Brucellosis, hepatitis, bisitopenia



Tuberculous Orchiepididymitis, Meningoencephalitis and Hydrocephalus

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Tuberculous meningoencephalitis (TBM) is a rare and serious, often fatal presentation of active tuberculosis and account for about 1% of cases. Early diagnosis and prompt treatment of TBM is essential to reduce morbidity and mortality.

Here, we report a case of TBM in 60-year-old man. TBM was considered on the basis of clinical presentation, laboratory findings (hyponatraemia) cerebrospinal fluid studies, radiological findings (hydrocephalus on MRI of the brain), and history of orchiepididymitis of unknown origin one year earlier, together with information that the patient originated from Kosovo where incidence of tuberculosis is still high. *Mycobacterium tuberculosis* was cultured from cerebrospinal fluid on Lowenstein-Jensen medium confirming diagnosis of TBM. Subsequently, acid-fast bacilli (AFB) staining on samples obtained after orchiectomy a year ago was performed, revealing AFB. Anti-tuberculosis therapy is still in course.

This is the second case of tuberculous meningoencephalitis with the same disease pattern (i.e. tuberculous orchiepididymitis-meningoencephalitis) in our department, and this fact was crucial for the presumptive diagnosis and urgent treatment of TBM. The former case was described five years ago.

Key Words: Tuberculous orchiepididymitis, tuberculous meningoencephalitis, hydrocephalus



Weil's Disease in a Patient Presented with Multiorgan Failure

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INTRODUCTION: Leptospirosis is a worldwide common zoonotic disease seen worldwide. The most important leptospirosis reservoirs are rodents, predominantly rats. Although leptospirosis presents with a non-icteric form in almost 90% of the cases, Weil's disease characterized by fever, severe jaundice, tendency to bleeding and fulminant hepatorenal failure can be seen in approximately 10% of the infected persons. Herein we report a case of Weil's disease, presenting with severe jaundice, calf pain, thrombocytopenia and acute renal failure.

CASE: A 20-year-old previously healthy male farmer with travel history presented our hospital with a history of fever, severe jaundice and bilateral calf pain that began five days prior. He had anemia, leukocytosis, thrombocytopenia, hyperbilirubinemia, elevated liver enzymes and acute renal failure at the presentation. Since he had risk factors such as being a farmer and history recent travel and clinical signs, Weil's disease was considered for this patient. Empirical ceftriaxone treatment was started (2 g/day) and a significant clinical response was observed. Microscopic agglutination test (MAT) was used for definitive diagnosis. He was discharged with cure.

CONCLUSION: Weil's disease is an important disease that can be associated with high mortality when diagnosis and treatment are delayed. Although it has not as high incidence in Turkey as in tropics a careful assessment of risk factors in the history of the patient with nonspecific clinical and laboratory findings should be performed for early diagnosis of leptospirosis that is critical for the course of the disease.

Key Words: Weil's disease, jaundice, thrombocytopenia, multiorgan failure



Pulmonary Brucellosis Detected During Treatment of Active Tuberculosis in a Patient with Operated Lung Cancer

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Brucellosis is an infectious disease with rare manifestation of pulmonary involvement. Diagnosis is rather difficult due to uncommon and nonspecific symptoms regarding to pulmonary involvement. The patient with pulmonary malignancy, initially diagnosed as active pulmonary tuberculosis. During antituberculosis therapy, pulmonary brucellosis developed.

The patient with diagnosis of pulmonary malignancy with pathologic stage II epidermoid carcinoma after surgery, came to chest disease clinic presenting with complaints of cough, sputum, fever and night sweats. In sputum examination asidoresistant bacillus (ARB) was detected and antituberculosis therapy was started. The symptoms regressed but, at fourth month of therapy patient represented with cough, fatigue, night sweat, weight loss and fever. Fibronodular infiltration in right lower zone was detected in chest X-ray. Sputum examination for ARB was negative. Bronchoscopy has been performed. Bronchial lavage examination was negative for ARB and pathological evaluation of biopsy was nondiagnostic. But in blood culture gram-negative coccobacilli was detected. Bronchoscopic examination was repeated with suspect brucellosis. *Brucella* agglutination test has been performed from bronchial lavage fluid, was found positive at 1/320 titer. Simultaneously performed serum brucella agglutination test result was 1/640. The case has been diagnosed as pulmonary brucellosis. Streptomycin and doxycycline therapy was started. Rapid clinical recovery was seen within five days and radiological recovery was obtained at the end of second week of treatment.

In our case, previous diagnosis of pulmonary carcinoma and tuberculosis had concealed diagnosis of pulmonary brucellosis. In conclusion, especially in endemic regions for patients presenting with nonspecific symptoms, brucellosis should be considered in differential diagnosis.

Key Words: Brucellosis, tuberculosis, malignancy

Prognostic Significance of Transforming Growth Factor-Beta 1 in Chronic Hepatitis C Infection

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OBJECTIVES: Interferon treatment is expensive and has various adverse effects. Some markers may help in making decision to stop or maintain the treatment. The aim of this study was to evaluate the effectiveness of serum transforming growth factor beta 1 (TGF-β1) in assessing outcome of interferon treatment in patients with hepatitis c virus (HCV) infection.

MATERIALS and METHODS: Twelve patients with chronic hepatitis C infections included in the study as treatment group [Group 1: Anti-HCV (+), HCV-RNA (+), damage scores for liver biopsy ≥ 4, fibrosis ≥ 2] and 12 patients with anti-HCV positive, HCV-RNA negative and normal liver function tests included as control group (Group 2). HCV-RNA levels were determined by realtime-PCR and TGF-β1 levels were measured with ELISA methods, at the beginning and 24th week of the treatment. Mann-Whitney U test and Wilcoxon test were used to compare variables within and between groups.

RESULTS: Median age and male/female ratios were 46 years and 5/7, and 45 years and 3/9 for Groups 1 and 2, respectively. Although no difference was found in TGF-β1 levels at the beginning of the treatment between Group 1 and Group 2 ($p > 0.05$), significantly decreased TGF-β1 levels were observed following 24 weeks of interferon treatment in group 1 ($p = 0.015$) (Table 1).

CONCLUSION: Despite limited number of patients, our data suggested that, TGF-β1 levels may be used as a prognostic marker for effectiveness of interferon treatment in patients with hepatitis C virus infection.

Key Words: Chronic hepatitis C infection, TGF-β1, interferon, prognosis

Table 1. TGF-β1 levels between two groups at the beginning and at 24th week (mean ± SD)

	Group 1 (n= 12)	Group 2 (n= 12)	p
At the beginning (n= 12)	13.70 ± 5.85*	12.30 ± 7.65	0.453
Responding to treatment, ng/mL (n= 11)	14.46 ± 5.47**	NA	0.396
Not responding, ng/mL (n= 1)	13.72 ± 8.26	NA	
At 24 th week (n= 12)	8.70 ± 4.28*	NA	NA
Responding to treatment, ng/mL (n= 11)	9.25 ± 4.54**	NA	0.683
Not responding, ng/mL (n= 1)	7.25 ± 3.88	NA	

NA: Not applicable; * $p = 0.015$, ** $p = 0.025$



Role of Magnetic Resonance Imaging (MRI) in Early Diagnosis of Acute Meningoencephalitis

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INTRODUCTION: Some cases of acute meningoencephalitis are not always clear in their subjective and objective status concerning certain etiological agents and certain age groups of patients. Hence they pose differential diagnostic dilemmas.

AIM: The aim of this study is to point out a role of MRI in early diagnosis of acute meningoencephalitis.

METHODS: We analyzed 23 patients diagnosed with acute encephalitis among various age groups, with or without etiological confirmation of disease. The median time of performing of MRI was 13.3 days upon the day of admission.

The benefit of MRI was expected in cases with altered consciousness, seizures, prolonged fever with pleocytosis and proteinorachia in cerebrospinal fluid (CSF), cases with neurological deficit and mental alteration.

RESULTS: MRI changes were pathognomic for meningoencephalitis in 19 of 23 patients (82.6%).

DISCUSSION: MRI is the most sensitive method in neuroradiological diagnosis of acute meningoencephalitis. It can detect changes in the initial phase of the disease, as well as signs of complication.

CONCLUSION: Specificity of MRI compared to the other diagnostic methods is indicative for its early performing.

Key Words: Acute meningoencephalitis, MRI, diagnosis



Pseudomonas aeruginosa and *P. fluorescens* Infections Associated with Retroperitoneal Abscess

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BACKGROUND: Retroperitoneal abscess is a relatively rare condition. A search of the literature reveals none reported case of *P. aeruginosa* and *P. fluorescens* infections associated with retroperitoneal abscess.

CASE: A 41-year-old man presented with a one-year history of abdominal pain radiating to the right flank. He had undergone right nephrectomy 10 years ago due to atrophic kidney. The hematocrite was 42 percent; serum sodium, 142 mEq/L; potassium, 4.1 mEq/L; creatinine, 1.2 mg/dL; BUN, 15 mg/dL; and WBC count 12.400/ μ L. On ultrasonography and computed tomography, 12 x 6 cm multiloculated retroperitoneal abscess was seen. USG guided percutaneous nephrostomy was inserted and 250 mL yellow-green drainage was obtained at the time of initial implementation. *P. aeruginosa* and *P. fluorescens* were identified by automated Vitek II (bioMérieux) microbial identification system from the abscess material. The antibiotic susceptibility tests were also performed with the same system. *P. aeruginosa* was susceptible to ticarcillin-clavulanic acid, ceftazidim, cefepim, imipenem, meropenem and ciprofloxacin. On the other hand, it was resistant to gentamicin, amikacin and tetracyclin. *P. fluorescens* was susceptible to ticarcillin-clavulanic acid, cefepim, imipenem, meropenem and ciprofloxacin. On the other hand, it was resistant to ceftazidim, gentamicin, amikacin and tetracyclin. The patient was started on parenteral ticarcillin-clavulanic acid and ciprofloxacin.

CONCLUSION: To our knowledge, this is the first case of *P. aeruginosa* and *P. fluorescens* infections associated with retroperitoneal abscess after open right nephrectomy. More than one microorganism can be active simultaneously in infections such as soft tissue abscess. This study; is presented to contribute to the literature since it demonstrated that microorganisms from the same genus but from different species may lead co-infection.

Key Words: Co-infections, *P. aeruginosa*, *P. fluorescens*, retroperitoneal abscess



***Serratia ficaria* Isolated from Sputum Specimen**

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BACKGROUND: *Serratia ficaria* was first described in 1979 by Grimont et al. This bacterium was found in figs but also isolated from human specimens in a few cases. We now report an isolate of *S. ficaria* from sputum.

CASE: A 46-year-old man presented with a five-year history of chronic renal failure, four months of peritoneal dialysis and one week of fever with respiratory tract infection, accompanied by cough. His body temperature was 37.8°C. The hematocrite was 32.59 percent; serum sodium, 135 mmol/L; potassium, 3.9 mmol/L; chloride, 96 mmol/L; creatinine, 10.2 mg/dL; BUN, 58 mg/dL; CRP, 206 mg/L, and WBC count 17.95 K/ μ L. Sputum culture yielded a growth of gram-negative rod. It was identified as *S. ficaria* based on the following criteria: fermentation on glucose oxidation-fermentation medium, weak fermentation on MacConkey agar, motility and acid production in TSI agar, and by automated Vitek II (bioMérieux) microbial identification system. The antibiotic susceptibility tests were also performed with the same system and by the disk diffusion method on Mueller-Hinton agar with 24 h of incubation at 35°C. *S. ficaria* was susceptible to amikacin, gentamicin, cefepim, trimethoprim-sulfamethoxazole, imipenem, meropenem and ciprofloxacin. On the other hand, it was resistant to ampicillin, amoxicillin-clavulanic acid, ceftiofloxacin, cephalothin. The patient was treated successfully.

CONCLUSION: *S. ficaria* is an opportunistic pathogen responsible for colonization or serious infections in compromised patients. This bacterium is found in figs and in the specific fig pollinator *Blastophaga psenes*. The fig tree and fig play an important role in human colonization. It should be kept in mind that *S. ficaria* infections may be encountered frequently especially in fig tree epidemic regions.

Key Words: Figs, infections, *Serratia ficaria*, sputum



Electroencephalographic Abnormalities as a Predictor of Distinguishing Acute Meningitis and Encephalitis

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BACKGROUND: Distinguishing meningitis from encephalitis in clinical practice is mainly based on the patient's state of consciousness or the presence of acute neurological or mental deficit. The aim is to determine what is the predictive value of EEG in the differentiation of acute meningitis from encephalitis (meningoencephalitis) as a clinical diagnosis.

MATERIALS and METHODS: We analyzed 45 EEG records of patients hospitalized at the clinic for infectious diseases, with meningitis and meningoencephalitis in four-year period, taking into account the state of consciousness and CSF findings in the initial period of hospitalization.

RESULTS: Twenty four patients with normal state of mind had a normal EEG in 58% of cases, confounding the patients was 13, of which 5 patients (38%) had severe EEG recording medium and 5 patients (38%) of small degree. Patients with sopor was 6, with prevalence of 50% and severe EEG changes. One patient was in a coma and had severe EEG changes, one was with small degree of EEG findings with specific Graph elements with clinical manifestation of seizures.

CONCLUSION: The findings of the degree of abnormality in the EEG of acute CNS infection may be a predictor of involvement of brain parenchyma and subsequently in the differentiation meningitis from encephalitis.

Key Words: Acute meningitis, acute encephalitis, an electroencephalogram (EEG)



Analysis of CSF Findings with Reference to Antibiotic Therapy of the Meningococcal Disease

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Meningococcal disease has been known for two centuries, but still there are many issues related to the understanding, prevention and treatment of this disease and until a respond to them, meningococcal infection remains a major problem among the human population.

OBJECTIVE: To analyze the CSF findings of patients with meningococcal disease with reference to therapy.

PATIENTS and METHODS: We analyzed patients treated at the clinic for infectious disease during the five year period.

RESULTS: Fifty three patients were included, of which 49% with the clinical picture of meningococcal sepsis, 40% with sepsis and meningitis and 11% with meningitis. Wilcoxon's rank test showed that the differences in the mean (median) number of cells, protein and glucose level between the first and control CSF findings are statistically significant. Ceftriaxon monotherapy was prescribed in 32% of patients, a combination (ceftriaxon, chloramphenicol and crystacillin) in 68%. Mann-Whitney test showed that the difference (median) in length of hospital stay between patients treated with combination and monotherapy is statistically significant.

CONCLUSION: In the analyzed sample clinical form of meningococcal meningitis was found in the smallest number of patients with meningococcal disease. Following the findings of CSF we demonstrated that the initial antibiotic therapy was adequate and that the length of hospitalization patients treated with monotherapy was shorter.

Key Words: Meningococcal disease, meningitis, CSF, antibiotic therapy



Acinetobacter baumannii Infections in Burn Unit of a University Hospital

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Recently, acinetobacter infection is accepted as one of the leading causes of morbidity and mortality in patients with burn. It may cause delay in wound healing, graft loss and sepsis. In this study, we aimed to report the treatment modalities and their results in cases with proven *Acinetobacter baumannii* infection in burn area.

Totally, 44 burn patients that *A. baumannii* were identified in their burn wound cultures and treated in Dicle University Burn Center between 2009-2011 were included. Age range of cases was between 3-54 years and burn surface area was between 10-60%. In addition, Colistin sensitive *A. baumannii* was isolated in 4 patients among blood cultures of the 8 patients with fever and increased white blood cell count. Prophylactic cefazolin was started in cases with burn surface area under 20% and ceftazidime-amikacin was started in those over 20%, in total of 44 patients. Surgical debridement and dressing with nanocrystalized silver impregnated products were also performed to all patients. Intravenous colistin was given to patients whose blood cultures were favourable for *A. baumannii*.

Except two patients, whose blood cultures were favourable for *A. baumannii*, no bacteria was found in wound cultures of patients after treatment. Two of four patients that acinetobacter was detected in their blood cultures die as a result of sepsis. The control blood cultures were unfavourable in other two cases.

Mortality and morbidity rates can be reduced in burn patients whose wound colonized with *A. baumannii*, by appropriate management before bacteria causing systemic infection.

Key Words: *Acinetobacter baumannii*, burn unit, burn wound, wound culture



***Serratia marcescens* Meningitis Following Spinal Anaesthesia and Arthroscopy**

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In this paper we present case of bacterial meningitis, occurred following spinal anaesthesia. Although very rare bacterial meningitis is serious complication of spinal anaesthesia and early diagnosis as well as effective treatment is extremely important. Leading pathogens listed as causative agents of meningitis related to spinal anaesthesia are streptococci. We present case caused by *Serratia marcescens* (ESBL) confirmed by culture in cerebrospinal fluid and blood, as an important signal and need for improvement of infection control measures.

Previously healthy individual, admitted to orthopaedic department for routine arthroscopy, approximately within 24 hours after operation was performed complained of headache and fever. Infectious diseases physician was consulted, lumbar puncture was performed and purulent meningitis was confirmed. Further treatment was done at clinic for infectious diseases. Cerebrospinal fluid and blood cultures of patient confirmed *S. marcescens*, resistant pathogen important intrahospital agent. Patient was successfully treated. Cases of spinal meningitis caused by *S. marcescens* are rare, and obviously local resistance pattern is important and should be always considered when starting therapy. Infection control team was appointed and after investigation discovered *Serratia* in anaesthetic vial used in procedures. New measures and recommendations regarding infection control were implemented at orthopaedic department.

Meningitis is a serious complication and early diagnosis and early treatment is extremely important. Meningitis should always be considered as a possible differential diagnosis with patients after spinal anaesthesia complaining on headache and fever. Knowledge and practice of infection control measures is mandatory and should be always emphasized to performing staff.

Key Words: *Serratia marcescens*, meningitis, spinal anaesthesia



The Treatable Cause of Ataxia: A Case of Tabes Dorsalis

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INTRODUCTION: Tabes dorsalis is an infrequent form of neurosyphilis cases. Today, this is a rare and treatable cause of ataxia. This case is rare, due to late diagnosis and recovery with penicillin treatment was presented.

CASE: Thirty seven years male patient's gait disorder and leg pain began two years ago and had gradually increased. He entered the suspected sexual intercourse ten years ago. In neurological examination pathological signs; joint position sense were decreased, hypoactive deep tendon reflexes, gait ataxia, had romberg sign. FTA-Abs tests of blood and cerebrospinal fluid: positive, VDRL Syphilis: 17.12 S/CO unit (positive), respectively. HIV Ag/Ab: 0.10 (normal), S/CO unit, EMG, brain, thoracic and lumbar MRI was normal. Patient with infection diseases department was consulted, penicillin G 24 million units a day with their recommendation was given 14 days. Neurological examination findings were significantly improved after six months ataxia, romberg sign is absent. After six months of repeated blood VDRL test was negative.

CONCLUSION: Slowly progressive gait disorder, even today neurosyphilis should be considered. Early diagnosis and treatment is important because it is at today a rarely cause of ataxia.

Key Words: Ataxia, tabes dorsalis, treatment

An Evaluation of the Biochemical and Microbiological Findings of Patients with Pulmonary Tuberculosis

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INTRODUCTION: The fact that antituberculosis treatment is protracted and that a large number of many various drugs are used together increases the likelihood of drug-associated side-effects. These side-effects further encourage the "desire to quite drugs" existing in a significant number of patients. Monitoring biochemical markers is therefore of great importance in the treatment of patients with tuberculosis. This study was intended to determine biochemical markers pre- and post-antituberculosis treatment.

METHOD: The demographic characteristics and biochemical and laboratory findings of cases diagnosed as pulmonary tuberculosis at the Trabzon Ahi Evren Thoracic, Heart and Cardiovascular Surgery Training and Research Hospital in Turkey in 2007-2010 were evaluated retrospectively. Results were transferred onto SPSS and analyzed statistically.

RESULTS: One hundred twelve cases diagnosed with pulmonary tuberculosis were enrolled. Patients' average age was 50.9 ± 20.1 , and 89 (79.5%) were male. Smear (+) levels was 69.6%, with a culture positivity level of 83.9%. Of the biochemical markers, statistically significant changes were observed between white blood cell count (WBC), hemoglobin (Hb), platelet count (PLT), mean corpuscular volume (MCV), red-cell distribution width (RDW), sedimentation, C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and blood-urea-nitrogen (BUN) values pre- and post-treatment (Table 1).

CONCLUSION: There may be changes in biochemical markers before and after antituberculosis treatment administered to these patients. Prompt determination of these changes and appropriate therapy will increase patients' compliance with antituberculosis treatment. And this will contribute to the antituberculosis treatment itself.

Key Words: Tuberculosis biochemical findings antituberculosis treatment

Table 1. Laboratory characteristics of patients with pulmonary tuberculosis

Characteristics	pre-antituberculosis treatment	post-antituberculosis treatment	p
WBC ($10^3 \mu\text{L}$)	8900 ± 2600	7500 ± 2600	0.000
Hb (g/dL)	12.7 ± 1.8	13.2 ± 2.0	0.001
PLT ($10^3 \mu\text{L}$)	323.000 ± 107.000	271.000 ± 87.000	0.000
MCV (fL)	83.7 ± 6.9	85.8 ± 6.3	0.000
MPV (fL)	7.7 ± 1.0	7.7 ± 0.7	0.556
RDW (%)	12.5 ± 2.9	13.1 ± 2.0	0.000
PDW (%)	11.9 ± 2.6	12.0 ± 2.5	0.771
Sedimentation (mm/h)	68.7 ± 29.6	36.6 ± 30.7	0.000
CRP (mg/dL)	6.9 ± 5.9	4.2 ± 5.5	0.001
ALT (U/L)	25 ± 28	31 ± 26	0.027
AST (U/L)	28 ± 24	30 ± 22	0.016
BUN (mg/dL)	35.5 ± 14.0	34.3 ± 16.4	0.029
Cr (mg/dL)	0.9 ± 0.3	0.8 ± 0.3	0.223
Total protein (g/dL)	7.2 ± 0.8	7.1 ± 0.7	0.745
Albumin (g/dL)	3.6 ± 0.6	3.7 ± 0.7	0.064



Evaluation of Tick Bite Cases Admitted to the State Hospital

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OBJECTIVE: Crimean-Congo hemorrhagic fever (CCHF) is a serious viral infectious disease, which is characterized by fever and bleedings in the body, and associated with 5% mortality. Usually, it spreads by tick bites. However, CCHF can be transmitted by contact with the infected human or animal blood or tissues. In this study, CCHF disease which is an important health problem in our country was evaluated epidemiologically.

METHOD: Tick bite cases admitted to the State Hospital of Tokat between 1 April and 30 September, 2009 were assessed in terms of CCHF incidence and clinical features in an epidemiological study.

RESULTS: 312 cases of tick bites have been included to the study. 182 of these cases were men and 130 of them were female. Of the cases, 21.1% was under the age of 16 years old and the mean age was determined as 34.4 ± 14.6 . 56.4% of the cases were living in urban area and the most of the cases have been visited these places. The most common body area bitten by the ticks were the lower extremities. The most cases of the tick bites were recorded in May, June, July and August, CCHF developed in 8 cases.

CONCLUSION: Cases of tick bites should be monitored carefully in terms of symptoms and signs in endemic areas where CCHF is seen. People living in these regions, should be trained in terms of measures to be taken against tick bite, and the applications after tick bite.

Key Words: Tick bite, Crimean-Congo hemorrhagic fever, epidemiology



Clinical Aspects of Human Brucellosis

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INTRODUCTION: Brucellosis is a multi-systemic infection in which any organ or system of the body can be involved. After the appearance of first cases of human brucellosis in Bosnia and Herzegovina in the year 2000, it has become a serious, growing public health problem.

AIM: To examine the frequency, types, clinical features and outcome of the most commonly localized forms of human brucellosis.

PATIENTS and METHODS: We retrospectively analyzed 120 cases of brucellosis who were diagnosed and treated at the Clinic for Infectious diseases in Sarajevo during two years period. The diagnosis was made by clinical findings, and confirmed by the serologic tests and/or the isolation of *Brucella* species.

RESULTS: The cause of brucellosis in this area is *B. melitensis*, and to a small extent *B. abortus*. The disease is diagnosed late, on average in the middle of the third month (73.9 ± 99.1 days). Localised forms of brucellosis prevail (73.3%) over non-localised. Osteoarticular manifestations are the most common localised forms of the disease (57.5%). Orchiepididymitis was the most common non-joint manifestation of brucellosis (10.8%).

CONCLUSIONS: A long period of diagnosis has been an important predictor of localised forms, occurrence of spondylitis and the final outcome of the disease. Although the number of patients with brucellosis presenting at our clinic has reduced, continuous organized effort is necessary for brucellosis control.

Key Words: Human brucellosis, clinical features, complications



Organic Targets in Staphylococemia

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Staphylococemia the presence of staphylococci in circulating blood. Continuous or intermittent penetration of agents in the blood from septic foci and metastasis formation (which may occur in any organ) are contributing the mostly for the development of sepsis. The aim of this article was to determine the most common metastatic foci within the staphylococcal sepsis. Available medical histories of 18 patients hospitalized at the Clinic for Infectious Diseases, Clinical Center of Sarajevo were retrospectively evaluated in the two-year period (2009-10) Those who had positive blood cultures on staphylococci (MSSA, MRSA, MRSE). Most metastases have been described in lung at 8 patients (44%), followed by bone and soft tissues also at eighth patient, while in the rest patients, intrabdominal abscesses, endocarditis and skin metastases were found. Expected correlation between age and metastatic foci has not been shown. The concept of therapy was modified according to the availability of antibiotics, clinical course and metastases in within staphylococcal sepsis.

Key Words: Staphylococemia, sepsis, pneumonia, metastasis



Infective Endocarditis: Evaluation of 49 Cases

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OBJECTIVES: It was aimed to evaluate clinical and laboratory features of 49 infective endocarditis (IE) patients who were followed in our hospital due to Modified DUKE criteria.

METHODS: We prospectively evaluated clinical and laboratory findings of 49 patients treated for IE between June 2006 and April 2010 in our hospital. Modified Duke Criteria were used for the diagnosis of IE.

RESULTS: There were a total of 49 patients (29 male, 20 female, aged 53.65 ± 17.48 range 20-83). Of 49 cases 45 (89.7%) had left sided endocarditis whereas four had right sided endocarditis. Furthermore 40 of them native valve and 9 of them were artificial valve endocarditis. Most of the patients had co-morbidities; mitral valve replacement (6), past IE history (4), other cardiac pathologies (20), chronic renal failure (8), diabetes mellitus (3), tuberculosis (3), connective tissue disorder (2), chronic obstructive pulmonary disease (1) and alcoholism (1). In terms of clinical findings headache was most common among patients (47) and followed by fatigue (27), weight loss (23), dyspnea (19), petechia (4) and necrosis of fingers (1). Blood culture yielded a pathogen in 41 of 49 patients (83.6%). Pathogens were *Streptococcus viridans* (14), *Staphylococcus aureus* (7), *Enterococcus* spp. (7), coagulase-negative staphylococci (4), *Streptococcus mitis* (2), *Streptococcus gordonii* (2), *Streptococcus sanguis* (1), *Brucella melitensis* (1), *Escherichia coli* (1), mould (1) and *Corynebacterium* spp. (1). According to modified Duke Criteria; 44 patients had definitive and five patients had possible IE diagnosis (Table 1). Vegetation was observed by echocardiography in 44 of 49 IE patients (89.8%). Forty two patients were successfully treated by proper medical and surgical treatment. Overall mortality was 14.3% (7 patients).

CONCLUSION: IE is a serious and life threatening infection. The clinic findings can be different because of the underlying diseases and risk factors. Modified Duke criteria are useful for diagnose and treatment.

Key Words: Infective endocarditis, risk factors, Duke criteria

Table 1. IE diagnose according to modified Duke criteria

Duke criteria	n	%
Definite IE	44	89.8
2 Major	35	
1 Major + 3 Minor	9	
Possible IE	5	10.2
1 Major + 1 Minor	3	
3 Minor	2	



Distribution of Mycobacteria Other Than Tuberculosis in Different Geographical Regions of Turkey

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INTRODUCTION: Mycobacteria other than tuberculosis (MOTT) can cause severe infections especially in immunosuppressed patients. Early diagnosis of those strains is particularly important to determine correct therapeutic approach. It is important to identify the strains to the species level to help the clinician for choosing the right drug. In this study, we aimed to determine species distribution of 90 MOTT isolated from four geographical regions.

METHOD: We sequenced 441 base pair of Hsp65 gene and 1030 base pair of 16S rRNA region of 90 MOTT strains isolated from four regions between 2001-2008. Results were analysed by comparing Gene Bank data.

RESULTS: The three most common type were *M. gordonae* (n= 21), *M. abscessus* (n= 13), *M. lentiflavum* (n= 9) , whereas there was only one *M. flavescens*, *M. mucogenicum*, *M. chelonae*, *M. elephantis*, *M. terrae*, *M. xenopi*. The most common type was *M. abscessus* (n= 6) in 11 strains from Istanbul, *M. kumamotoense* (n= 6) in 19 strains from Ankara, *M. abscessus* (n= 6) in 20 strains from Malatya and *M. gordonea* (n= 14) in 40 strains from Samsun.

CONCLUSION: We may conclude that the distribution of MOTT strains vary in different geographical regions of Turkey.

Key Words: MOTT, geographical distribution

Distribution of Microorganisms That Isolated from Urine Samples in One Year Period

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INTRODUCTION: Urinary tract infections are the most common infection both in community and hospitalized patients. The most common microorganisms are *E. coli*, *Enterococcus* spp., *Klebsiella* spp., *Proteus* spp., *Staphylococcus* spp. But in hospitalised patients these microorganisms are also infection agents in addition to them *P. aeruginosa*, *Acinetobacter* spp., *Citrobacter* spp. and *Candida* spp. are also infection agents. In this study, our aim is to detect the frequency of the microorganisms that isolated from urinary tract infections in outpatients and inpatients individuals.

MATERIALS and METHODS: The bacterial isolates were reviewed retrospectively, which were isolated from urine samples presented to microbiology laboratory of Ondokuz Mayıs University Medicine School teaching hospital between January 2009-January 2010. The identification of the bacterial isolates was done by Vitek2 system (Biomérieux, France) and BD Phoenix (USA) and biochemical methods. The results were interpreted in statistical analyse according to the two proportion test in Minitab 16 program.

RESULTS: In one year period (January 2009-January 2010) we have reviewed 2939 outpatients urine samples and 4235 inpatients urine samples results. In outpatients *S. agalactiae*, *E. coli*, coagulase-negative staphylococci were found statistically significant to inpatients and in inpatients *Acinetobacter* spp., *E. faecium*, *K. pneumoniae*, *P. aeruginosa*, yeasts, *Citrobacter* spp. were found statistically significant to outpatients.

CONCLUSION: It has been already known that some microorganisms are seen in the hospital more than in community. These microorganisms are frequently causative agent of hospital-acquired infections. These infections increase the mortality and morbidity, cause prolonged treatment and increase the cost of treatment. Because of this it is important to know the causative agent of hospital-acquired infections for the development treatment policy in hospitals. In our hospital *Acinetobacter* spp., *E. faecium*, *K. pneumoniae*, *P. aeruginosa*, yeasts, *Citrobacter* spp. were found significantly more than from community. While *Acinetobacter* spp., *K. pneumoniae*, *P. aeruginosa*, *Citrobacter* spp. have broadspectrum antimicrobial resistance and *E. faecium* is important for the vancomycin resistant isolates, they have importance in the hospitalised patients. We think that it is important to pursuit regularly ratio of these microorganisms.

Key Words: Urine samples bacterial isolates, inpatients, outpatients



Distribution of *Enterococcus* Species Isolated from Various Clinical Specimens

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INTRODUCTION: Enterococcal infections have increasing importance in nosocomial and community acquired infections. *Enterococcus* strains are mostly isolated from urinary tract infections. The objective of this study is evaluation of isolated *Enterococcus* species over a 5-year period in Ondokuz Mayıs University Hospital.

MATERIALS and METHODS: The specimens from the outpatients and inpatients in Ondokuz Mayıs University, Medical Faculty Hospital between 2006 and 2010 were inoculated onto routine culture media (5% sheep blood agar, eosin metilen blue agar). After incubation at 37°C for 18-24 hours, colony morphology, Gram stain characteristics and catalase activity were evaluated. Identification of the enterococci suspected isolates were performed by BD Phoenix (Becton-Dickinson, USA) and Vitek 2 (Biomerux, France) automated systems. Repeated isolates were excluded from the study.

RESULTS: Totally 3916 *Enterococcus* strains were isolated. The isolation site distribution of *Enterococcus* strains were as follows; 2397 urine, 645 blood, 262 swab (wound, vaginal etc.), 215 sterile body fluid (except cerebrospinal fluid), 122 aspirate (deep wound, discharge etc.), 110 catheter, 75 cerebrospinal fluid, 47 tracheal aspirate, 30 sputum and 13 bile. Most of the clinical specimens were obtained from internal medicine departments 681 (17.3%). The species of *Enterococcus* strains were as follows; 2213 (56.51%) *Enterococcus faecalis*, 1652 (42.19%) *Enterococcus faecium*, 15 (0.39%) *Enterococcus durans*, 14 (0.35%) *Enterococcus casseliflavus*, 13 (0.33%) *Enterococcus gallinarum*, 7 (0.18%) *Enterococcus avium* and 2 (0.05%) *Enterococcus hirae*.

CONCLUSION: Our study showed that urine and blood samples are higher than other clinical samples. Also, among all of the isolates of enterococcus, *E. faecalis* and *E. faecium* strains were found more frequently than other enterococcus species.

Diagnostics

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The False Sero-Negativeness of Brucella Standard Agglutination Test: Prozone Phenomenon

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AIM: We aimed to discuss prozone phenomenon that is quite rare and causes false negativeness in serological diagnosis of brucellosis with standard dilution titers.

METHOD: In this study the tests of 4 cases were evaluated. Blood cultures were obtained from all cases while cerebrospinal fluid cultures were studied in the two cases. Rose Bengal, standard agglutination and coombs' tests were applied to all patients.

RESULTS: Rose Bengal test were negative in all cases; standard agglutination test (SAT) and coombs' test were negative in titers up to 1/640. The Rose Bengal, SAT and coombs' tests in cerebro spinal fluid (CSF) of the two cases with neurobrucellosis diagnosis were negative, as well. Since the clinical and laboratory findings suggested the brucellosis, the serums were restudied by diluting up to 1/10240 titer and we saw that the first 3 cases became positive at a titre of 1/1280. The fourth case remained negative and therefore, we applied high dilution coombs' test. This time the test gave a positive result at 1/10240 titer beginning from 1/2560 titer. *B. melitensis* was isolated from the CSF of the first case on the 7th day and from blood of the fourth case on the 6th day. The remaining tests of the cases were normal.

CONCLUSION: In order to exclude false sero-negativeness in cases with clinical and laboratory findings strongly suggesting brucellosis, coombs' test and SAT should be studied by diluting up to a titer of 1/2560 and over.

Key Words: Brucellosis, prozone phenomenon, standard agglutination test, coombs' test

Table 1. The culture and serological test results of the cases

Case	Rose Bengal	SAT positive titer	Coombs' test positive titer	SAT result	Coombs' result	Culture result
1	Negative	1/1280	1/1280	1/2560	1/2560	<i>B. melitensis</i>
2	Negative	1/1280	1/1280	1/5120	1/5120	
3	Negative	1/1280	1/1280	1/2560	1/2560	
4	Negative	Negative	1/2560	Negative	1/10240	<i>B. melitensis</i>



Can Procalcitonin Help the Diagnosis of Osteomyelitis in Adults? A Prospective Study

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AIM: The aim of this study was to evaluate the sensitivity, specificity and predictive values of procalcitonin in adults patients with osteomyelitis.

MATERIALS and METHODS: A total of 30 consecutive patients with osteomyelitis and 30 healthy controls were enrolled in this study. Procalcitonin was measured by an Enzyme-Linked Immunosorbent Assay (Ray Bio® Human Procalcitonin ELISA Kit, Norcross GA, USA). Values of PCT levels > 0.5 ng/mL were considered as high than normal.

RESULTS: The ratio of the female to male both in patients and the control group was 10/20. The mean age of the patients was 31.16 ± 15.32 years, while in control group 32.22 ± 14.32 years. 26 (86.7%) of the patients had clinical signs and symptoms of osteomyelitis. White blood cell count detected high in 5 (16.6%) of them, erythrocyte sedimentation rate was high in 20 (66.6%) of them and C-reactive protein was positive in 15 (50%) patients, but PCT levels found to be higher in all 30 (100%) patients (PCT > 0.5 ng/mL). The PCT test, with a 0.57 ng/mL cut-off value, had a sensitivity of 87%, a specificity of 86% and a positive predictive value of 87%. This cut-off value (0.57 ng/mL) is quite suitable in osteomyelitis patients.

CONCLUSION: The sensitivity, specificity, and positive predictive values of PCT test are more discriminative than the other acute phase reactants in the patients with osteomyelitis. Therefore, the PCT test can be used as a useful marker in the diagnosis of osteomyelitis.

Key Words: Procalcitonin, osteomyelitis

Comparison of the Diagnostic Values of the Three Different Stool Antigen Tests for the Non-Invasive Diagnosis of *Helicobacter pylori* Infection

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The aim of the study was to compare 3 stool antigen tests for diagnosis of *Helicobacter pylori* infection in adult patients with dyspeptic complaints before eradication therapy. We compared 2 enzyme immunoassays (EIAs: Premier Platinum *H. pylori* Stool Antigen [HpSA] Plus and *H. pylori* Antigen [HpAg]) and one immunochromatographic assay (*H. pylori* fecal antigen test/lateral flow chromatography) in detecting *H. pylori*. All the investigated stool antigen tests were made of monoclonal antibodies. We evaluated 168 adult patients with *H. pylori* infection by using 2 criterion standard methods (histological and rapid urease tests) together. The sensitivity and specificity were 90% and 91%, respectively, for the Premier Platinum HpSA Plus, 77% and 91%, respectively, for the HpAg, and 81% and 92%, respectively, for the *H. pylori* fecal antigen test, respectively. The best agreement between the criterion standard tests and the stool antigen tests used in the study was with the Premier Platinum HpSA Plus. Immunochromatographic assay based stool antigen test (*H. pylori* fecal antigen test) was found to be more sensitive than the EIA-based test (HpAg). One of the 2 important conclusions obtained from the study was that the Premier Platinum HpSA Plus was found to be the most accurate test for the diagnosis of *H. pylori* infection in adult dyspeptic patients before eradication therapy, and the other was that monoclonal and high-quality, reliable immunochromatographic assay tests are a good option especially for small hospital laboratories that do not have appropriate equipment for performing the EIA and working on few samples.

Key Words: *Helicobacter pylori* infection, histopathology, rapid urease test, stool antigen test

Table 1. The test performances of the three HpSA tests as compared with the reference method

	Premier Platinum HpSA Plus-EIA	HpAg-EIA	<i>H. pylori</i> Fecal Antigen Test-LFC
Sensitivity (%)	90% (80-96)	77% (65-87)	81% (69-90)
Specificity (%)	91% (83-95)	91% (83-95)	92% (85-97)
PPV (%)	85% (74-92)	83% (71-91)	86% (75-94)
NPV (%)	94% (88-98)	87% (80-93)	89% (81-94)
Accuracy (%)	90% (85-94)	86% (80-90)	88% (83-92)
Total positive (n)	66	58	58
False-negative (n)	3	7	6
False-positive (n)	5	5	4

PPV: Positive predictive value, NPV: Negative predictive value.



Culturel Positivity of TB Pleuritis in Sarajevo Canton in Period 2004-2009

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INTRODUCTION: According appearance, pleuritis of TB etiology can be serous, serofibrous and rarely hemoragic and purulent. Inflammatory changes of pleura are caused with *M. tuberculosis* and in diagnostic purpose, they are getting material with pleural punction. That material is sawn on microbiological media.

PURPOSE: To show number of positive isolates of pleural punction on *M. tuberculosis* in relation to number of epidemiologically reported cases of TB pleuritis in Sarajevo Canton.

MATERIALS and METHODS: In this work, we used samples of pleural punctions sent to microbiological diagnosis in Sarajevo Canton. We used cultivation methods on solid Loewenstein-Jensen and liquid BACTEC MGIT 960 media.

RESULTS: In this work we involved results of analysis of pleural punctions in period 2004-2009. In 2004, out of 21 registered TB pleuritis, with 3 (14.2%) patients *M. tuberculosis* is proved. In 2005, out of 19 registered TB pleuritis, *M. tuberculosis* is proved with 6 (31.5%) patients. In 2006, out of 11 registered TB pleuritis, *M. tuberculosis* is proved with 3 (27.2%) patients. In 2007, out of 23 registered TB pleuritis, *M. tuberculosis* is proved with 13 (56.5%) patients. In 2008, out of 17 registered TB pleuritis, *M. tuberculosis* is proved with 11 (64.7%) patients. In 2009, out of 19 registered TB pleuritis, *M. tuberculosis* is proved with 12 (63.1%) patients.

CONCLUSION: Comparing results of analysis in this period, obvious is rise of culturel positivity of pleural punctions in period 2007-2009, what we can attribute to implementation of liquid BACTEC MGIT 960 media in diagnosing mycobacteria.

Key Words: *M. tuberculosis*, pleuritis



Evaluation of Rapid Immunochromatographic Test and ELISA in the Diagnosis of *Entamoeba histolytica*

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INTRODUCTION: Humans are infected by two morphologically identical species of *Entamoeba*. *Entamoeba histolytica* is the cause of amebic colitis and liver abscess, and *Entamoeba dispar* is noninvasive. The aim of this study was to estimate the true prevalence of *E. histolytica* by stool adhesin antigen detection method that distinguish *E. histolytica* from nonpathogenic *E. dispar* which previously microscopically identified *E. histolytica*-*E. dispar* complex on stools of patients.

MATERIALS and METHODS: Stool samples were collected from diarrheic patients in January 2011-February 2011 at the Meram Faculty Hospital of Selcuk University. *E. histolytica/dispar* complex was detected 34 (1.5%) of 630 stool specimens by nativ-lugol examination. Positive stool specimens which were detected using the nativ-lugol method were examined by the immunochromatographic rapid assay and *E. histolytica* specific adhesin antigen based ELISA test method.

RESULTS: Of these 630 specimens, 34 (5.3%) specimens were positive for *E. histolytica/E. dispar* trophozoites/cysts microscopically using nativ-lugol method. Of these 34 specimens, 13 (38.2%) specimens were found to be positive for the immunochromatographic rapid assay and 2 (5.8%) *E. histolytica* by the adhesin antigen based ELISA test.

CONCLUSION: Due to the low sensitivity of nativ-lugol method in the prediagnosis of amoebiasis, it is necessary to perform adhesin antigen based ELISA on the specimens in order to determine whether the patient should be treated or to prevent patients from being given an unnecessary treatment.

Key Words: *E. histolytica/dispar*, ELISA, antigen detection



The Comparison of IHA and Rapid Immunochromatographic Test in the Diagnosis of Hydatid Cyst

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Hydatid cyst is an illness which involves liver and lungs and lead to serious diseases caused by *Echinococcus granulosus* in sheep and cattle-raising areas. Several serodiagnostic techniques have been evaluated for the diagnosis of hydatid cyst disease. These techniques are Enzyme-Linked Immunosorbent Assay (ELISA), IHA (Indirect Hemagglutination Assay) and Indirect Fluoresan Antikor Assay (IFAT). Rapid immunochromatographic test provides qualitative detection of total antibodies against *E. granulosus* in serum or plasma samples. The aim of this study was to assess the efficiency of the rapid immunochromatographic test in referance of IHA.

In this study, It was prospectively collected one hundred patients' sera between June 2010 and February 2011. The serum samples were examined by a commercial Hydatidose Fumouze (Fumouze, France) for IHA and Virapid Hydatidosis (Vircell, Spain) for Rapid immunochromatographic test.

As a result, the specificity and sensitivity of commercial Rapid immunochromatographic test were found to be 100% and 88%. The titers of four patients which evaluated as negative with rapid immunochromatographic test was found to be 1/160 with IHA.

In conclusion, rapid immunochromatographic test can used for diagnosis, IHA can used for follow up titer in hydatid cyst diseases in routine practice.

Key Words: *Echinococcus granulosus*, IHA, immunochromatographic test

Enteropathogenic Bacteria Detected in Clinical Stool Samples in a Ten Year Period in Istanbul, Turkey

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OBJECTIVE: To investigate the bacterial pathogens in stool samples and determine their antibiotic susceptibility.

MATERIALS and METHODS: Stool samples were cultured on Mac Conkey agar, Hektoen Enteric agar, Selenit broth and gram-negative broth for *Salmonella* and *Shigella*, on blood agar for *Vibrio*, *Aeromonas* and *Plesiomonas* and on *Campylobacter* selective agar for *Campylobacter*. Identification of bacteria was conducted by conventional methods and antibiotic susceptibilities were determined by disc diffusion method according to Clinical and Laboratory Standards Institute criteria.

RESULTS: A total of 16.279 stool samples were included. Bacterial pathogens were recovered from 1176 (7.2%) samples. *Salmonella* spp., *Campylobacter* spp., *Shigella* spp., *Aeromonas* spp., *Vibrio* spp. and *Plesiomonas* spp. were isolated from 479 (2.9%), 387 (2.4%), 204 (1.3%), 92 (0.6%), 8 (0.05%) and 6 (0.04%) stool samples respectively. The most frequently isolated *Salmonella* serotype, *Shigella* species and *Campylobacter* species is *S. enteritidis* (60.1%), *S. sonnei* (60.3%) and *C. jejuni* (95.1%) respectively. The isolation rates of enteropathogens and their resistance to antibiotics are shown in the figure and table respectively. Of 312 *Campylobacter* isolates, 63.1% were ciprofloxacin resistant and 7.7% were erythromycin resistant. Ciprofloxacin resistance for *Campylobacter* spp. has increased from 45% to 71.1% between 2004-2010.

CONCLUSION: Although *Salmonella* is the most frequently isolated enteropathogen in Turkey, *Campylobacter* infections have emerged especially since 2007. Ciprofloxacin is the most effective antibiotic against *Salmonella* and *Shigella*. Co-trimoxazole resistance for *Shigella* and ciprofloxacin resistance for *Campylobacter* is very high in Turkey.

Key Words: Diarrhoea, enteropathogen, *Salmonella*, *Campylobacter*

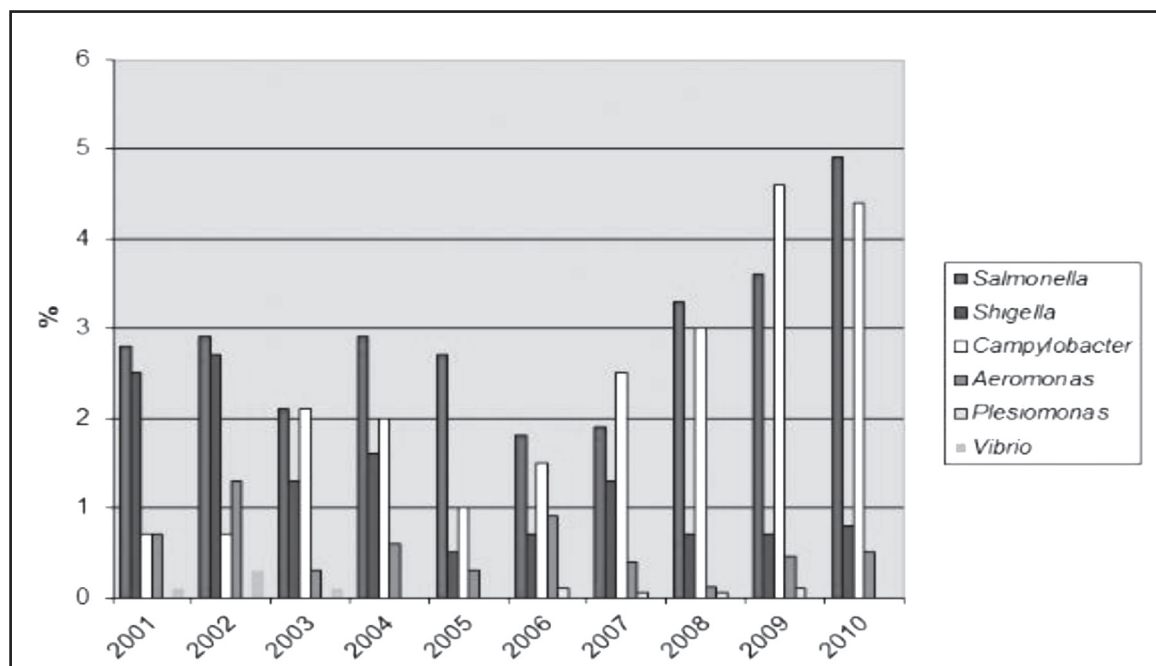


Figure 1. Isolation rates of enteropathogenic bacteria from 16279 stool samples.

Table 1. Microorganisms isolated from fecal samples and their resistance to antibiotics (n)

Microorganisms (n)	AM	SXT	CIP	CRO	FEP	AMC	C	NA
<i>S. enteritidis</i> (288)	29	17	1	7	4	14	1	-
<i>S. typhimurium</i> (66)	41	13	0	1	1	26	24	-
<i>S. typhi</i> (3)	1	1	0	0	0	0	1	-
<i>S. virchow</i> (1)	0	1	0	0	0	0	0	-
Group A <i>Salmonella</i> (3)	1	1	0	0	0	0	0	-
Group B <i>Salmonella</i> (13)	2	1	0	1	1	2	0	-
Group C <i>Salmonella</i> (54)	13	11	0	3	3	9	3	-
Group D <i>Salmonella</i> (7)	0	0	0	0	0	0	0	-
<i>Salmonella</i> spp. (38)	16	5	0	4	2	9	4	-
<i>S. arizona</i> (1)	0	0	0	0	0	0	0	-
<i>S. paratyphi</i> B (4)	3	0	0	0	0	1	0	-
<i>S. paratyphi</i> A (1)	1	0	0	0	0	1	0	-
Total n (%)	107 (22.3)	50 (10.4)	1 (0.2)	16 (3.3)	11 (2.3)	62 (12.9)	33 (6.9)	-
<i>S. sonnei</i> (124)*	19	97	1	4	2	10	-	4
<i>S. flexneri</i> (57)	43	19	0	1	1	29	-	4
<i>S. boydii</i> (13)	4	6	0	1	0	1	-	0
<i>S. dysenteriae</i> (10)	3	0	0	0	0	1	-	0
Total n (%)	69 (34.2)	122 (60.4)	1 (0.5)	6 (3)	3 (1.5)	41 (20.3)	-	8 (4)

* Antibiotic susceptibility testing was done for 122 isolates. AM: Ampicillin, SXT: Co-trimoxazole, CIP: Ciprofloxacin, CRO: Ceftriaxone, FEP: Cefepime, AMC: Amoxicillin-clavulanic acid, C: Chloramphenicol, NA: Nalidixic acid.



New Methods in Detection and Resistance Testing of *Helicobacter pylori*

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The golden standard to get information about possible resistances against antibiotics are culture with following resistance testing. *Helicobacter pylori* is know as fastidious and slow-growing bacterium, therefore growth can take several days. Although culture represents the most specific method for detection of *H. pylori* sometimes it is a problem to cultivate this bacterium. PCR is suitable for detection of organisms which are slow-growing and present in low numbers. Because of the fact that PCR provides results with high sensitivity, specificity and rapidity it could be an attractive alternative to culture. The aim of the present study was to compare results of culture followed by resistance testing via E-test with the results of *H. pylori* PCR using allele specific probes for resistance testing. Therefore we obtained 176 biopsies for PCR and culture. In 108 cases PCR was positive and resistance testing via PCR was possible in all cases. In culture 43 samples were positive, a following cultural resistance testing was possible in 19 cases. Compliance between resistance results of PCR and antibiogram was good. *H. pylori* PCR including allele specific probes for resistance testing seems to be an attractive alternative to cultural testing.

Key Words: *Helicobacter pylori*



Investigation of Influenza A and B Virus by Various Methods in Central Anatolia

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Influenza viruses cause seasonal epidemics associated with high morbidity and mortality and are important cause of respiratory diseases. In this study it is aimed to investigate influenza viruses by different methods in centre part of Turkey.

Nasopharyngeal swab samples were collected from clinics and outpatient clinics of Meram Medical Faculty Hospital of Selcuk University and different health care centers in Konya region during in November of 2008 and February of 2010. Rapid antigen test, shell vial cell culture test and PCR tests were studied for influenza A and B. Shell vial culture test was taken as gold standart and calculated the diagnostic values of other two tests for influenza A and B.

It was detected 31 (23.8%) influenza A and 10 influenza B (7.7%) positivity by standart diagnostic method. Sensitivity, specificity, positive predictive value and negative predictive value of rapid test of influenza A and B were 77.4%, 93.3%, 80.0%, 93.1% and 90.0%, 95.8%, 64.2%, 99.1% respectively. These values of multiplex PCR test of influenza A and B were 77.4%, 95.9%, 85.7%, 93.1% and 40.0%, 97.5%, 57.1%, 95.1% respectively.

Influenza A and B viruses are common cause of respiratory diseases. Due to rapid results within 48 hours, shell vial culture system was available for routine usage in regional diagnostic laboratory. Rapid antigen tests could be used for the management of influenza in both first and secondary health centers, especially when other viral studies are unavailable. Molecular diagnostic methods must be performed in tertiary health centers and reference laboratory.

Key Words: Influenza, diagnosis, PCR, rapid test, virus isolation

Assessment of Autoantibody Results Evaluated in Our Laboratory

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BACKGROUND: Autoantibody is an antibody, which were produced by immune system against organism itself. In this study, our aim was to investigate rate of autoantibody positivity in serum samples referred from various clinics.

MATERIALS and METHODS: In the present study, results of 9265 serum samples, which were referred to our laboratory between January 2007 and February 2011, were evaluated retrospectively. Among autoantibodies, anti-mitochondrial antibody (AMA), anti-nuclear antibody (ANA) and antibodies to double-stranded DNA (anti-ds DNA) were evaluated by Enzyme-Linked Immunosorbent Assay (ELISA) (TekTIME, Organon Tecnica, France).

RESULTS: Number of positive tests for all 3 antibodies was as follows: 110 of 4259 ANA tests, 67 of AMA tests and 172 of 3329 anti-ds DNA tests. Mean age was found as 42.0 ± 16.6 years (min 4-max 87) in ANA group, 44.8 ± 13.5 years (min 9-max 73) in AMA group and 43.1 ± 18.2 years (min 2-max 87) in anti-ds ANA group. Positivity according to gender is shown in Table 1 and positivity according to referring clinic is shown in Table 2.

CONCLUSION: It was found that positive cases were predominantly female in all 3 tests. It was seen that most of the positive cases for all three antibodies was from internal medicine, followed by Dermatology for ANA positivity and Neurology for AMA and anti-ds DNA positivity.

Key Words: Autoantibody, ELISA

Table 1. Autoantibody positivity according to gender

Gender	ANA		AMA		Anti-ds DNA	
	n	%	n	%	n	%
Women	93	84.5	50	74.6	126	73.3
Men	17	15.5	17	25.4	46	26.7
Total	110	100	67	100	172	100

ANA: Anti-nuclear antibody, AMA: Anti-mitochondrial antibody, Anti-ds DNA: Antibodies to double-stranded DNA.

Table 2. Autoantibody positivity according to referring clinic

Referring clinic	ANA		AMA		Anti-ds DNA	
	n	%	n	%	n	%
Pediatrics	2	1.8	1	1.5	6	3.5
Internal medicine	46	41.7	43	64.2	73	42.4
Ear-nose-throat	1	0.9	-	-	1	0.6
Physical therapy	16	14.5	1	1.5	22	12.8
Neurology	10	9.1	19	28.4	36	20.9
Ophthalmology	2	1.8	-	-	3	1.7
Dermatology	29	26.4	1	1.5	26	15.1
Orthopedics	4	3.6	-	-	4	2.3
Neurosurgery	-	-	-	-	1	0.6
General surgery	-	-	1	1.5	-	-
Obstetrics and gynecology	-	-	1	1.5	-	-
Total	110	100	67	100	172	100



Serological Diagnosis of Listeriosis

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OBJECTIVE: *Listeria monocytogenes* is gram-positive bacterium that can grow also at the temperature of 4 degrees C. Healthy animals can carry bacteria, but their meat and milk products are the source of infection of human being. The persons with weakened immunity, newborn infants and pregnant women are very much sensitive on infection with this bacteria. *L. monocytogenes* penetrates through the placenta and can lead to the fatal infection, which is characteristic by disseminated of a newborn and micro abscess on the placenta.

AIM: Find out if there is serological response by female patients in the reproductive age who had spontaneous abortion.

MATERIALS and METHODS: By agglutination serological method it had been researched if there is any antibody on *L. monocytogenes*. In testing were included 30 women in the reproductive age.

RESULTS: From the total of 30 patients positive samples were 18.

CONCLUSION: Serological diagnosis of listeriosis with agglutination/*Listeria* Gruber-Widal reaction/enables prompt diagnosis and the application of antibiotic therapy in cases of positive serologic response.

Key Words: *Listeria monocytogenes*, listeriosis, agglutination

Evaluation of Peritonitis Attacks Developed in CAPD Patients and Risk Factors for Peritonitis

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AIM: Peritonitis is the commonest complication seen periton dialysis. In this study, we aimed to evaluate the peritonitis attacks developed in CAPD patients, to identify the causative microorganisms and to determine their antibiotic susceptibilities and the risk factors for peritonitis.

MATERIALS and METHODS: The patients followed up in the periton dialysis unit of our hospital were enrolled in our study. 10 mL of periton dialysate fluid patients suspected of having peritonitis was inoculated into blood culture bottles and the sediment obtained after centrifugation of 40 mL fluid was inoculated on aerobic blood agar plates. Risk factors for peritonitis were evaluated in patients experiencing peritonitis

RESULTS: During the study, in 28 of 63 patients developed peritonitis attacks. The mean peritonitis incidence rate was 0.57 attacks/patient year. Growth occurred in 68.1% of the attacks. Although isolation rates were higher in blood cultures, there was no statistically significant difference between inoculation method on agar plates. The distribution of identified causative agents are shown in Table 1. Being older than 45 years old, living in country, lower education level, obligatory periton dialysis application and albumin levels lower than 3.5 g/dL were determined as risk factors for experiencing peritonitis.

CONCLUSION: In our study, significant difference was found between growth rates in blood culture systems and blood agar plates. CNS was the most frequently isolated agent. It is required that all centers should establish their correctable risk factors for development of peritonitis for their patient groups and take the preventive measures to decrease these peritonitis attacks.

Key Words: Periton dialysis, peritonitis, risk factors

Table 1. Distribution of the causative agents in culture positive peritonitis attacks

Causative agent	n	%
Gram-positive	24	75
Coagulase-negative staphylococci	12	37.5
<i>Staphylococcus aureus</i>	6	18.7
<i>Streptococcus</i> spp.	2	6.3
<i>Enterococcus faecalis</i>	4	12.5
Gram-negative	5	15.6
<i>Escherichia coli</i>	2	6.3
<i>Pseudomonas aeruginosa</i>	1	3.1
<i>Enterobacter cloacae</i>	1	3.1
<i>Acinetobacter haemolyticus</i>	1	3.1
Fungi	3	9.4
<i>Candida albicans</i>	2	6.3
<i>Candida parapsilosis</i>	1	3.1
Overall	32	100

The Importance of Early Diagnosis of HIV/AIDS and HIV Screening

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INTRODUCTION: Persons in whom the diagnosis is delayed are at greater risk of clinical progression, lower response to treatment. HIV/AIDS can be diagnosed earlier by means of screening tests. The aim of this study is to determine to ratio of early diagnosed HIV/AIDS patients and the effectiveness of screening tests in early stage.

METHOD: Clinical findings at admission and CD4 cell counts of 180 HIV/AIDS cases who were monitored in Infectious Diseases and Clinical Microbiology Department of Haseki Training and Research Hospital were analyzed retrospectively.

RESULTS: Of a total 180 HIV/AIDS cases, 149 (83%) were male and mean age of 36 years (range: 18-72 years). 71 (39%) patient presented with clinical signs and symptoms of HIV/AIDS while 109 (61%) were found to be HIV-positive in screening tests. The most frequent clinical symptoms on first admission were weight loss (17%), persistent generalized lymphadenopathy (16%) and oral candidiasis (16%). CD4 cell count was above 200/mm³ in 116 patients (61%), who were diagnosed in the early phase. Of these cases, 84 (72%) were asymptomatic and were diagnosed through voluntary or required screening tests. The association between causes of admission and CD4 cell counts of HIV/AIDS patients is shown in Figure 1.

DISCUSSION: Early diagnosis in HIV infection is essential for the health status of the patient and it can play a role in limiting HIV transmission. Screening for HIV is a very important strategy for reducing the number of the HIV-infected individuals who have not been diagnosed yet.

Key Words: HIV/AIDS, early diagnosis, screening tests

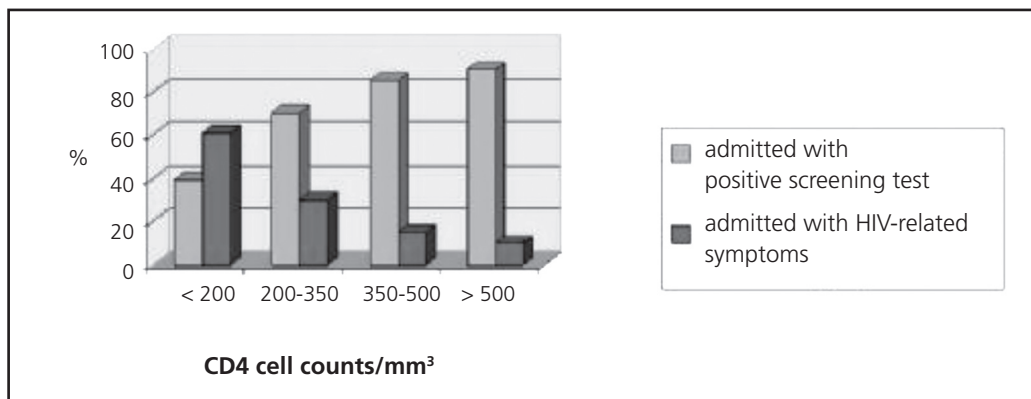


Figure 1. The association between admission causes and CD4 cell counts of HIV/AIDS patients.



Quantitative Analysis of *Brucella* spp. in Different Tissues of Aborted Bovine Fetuses Through Real-Time PCR

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Brucellosis, a bacterial disease caused by strains of the genus *Brucella*, is an important zoonosis. The infection is transmitted to humans by animals through direct contact with infected materials like aborted cattle fetus or indirectly by ingestion of animal products. In this study, *Brucella* spp. in different tissues of aborted cattle fetuses were analyzed quantitatively by real-time PCR. The material of the research composed 70 aborted cattle fetuses brought from cities in Eastern Mediterranean Region to Adana Veterinary Control and Research Institute Directorate between March 2008-March 2011. Genomic DNA amounts of *Brucella* spp. detected in brucellosis based wages' tissues, which were fresh, were putrefied and waited within formaldehyde (10%), were researched with real-time PCR. In 10 of 70 cattle fetuses, *Brucella* spp. were detected through real-time PCR and classical methods. Subcutaneous edema histopathologically was detected in fetuses where Brucellosis based wage developed, dark red color liquid accumulation was detected in cardiac and abdominal cavities and areas in colors changing from grey until dark red and having hard temper were detected in lungs. When tissues, the analysis of which was made with real-time PCR, were compared, it was seen that the sensitivity of the test decreased in tissues treated with formaldehyde more than in fresh tissues and that genomic DNA levels became lower. Moreover the DNA level in the lung tissue samples was detected in the ratio higher than in other tissues (liver, kidney, heart, spleen).

Key Words: Brucellosis, aborted fetus, real-time PCR



Coagulase-Negative Staphylococcal Peritonitis in Patients on Peritoneal Dialysis

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Peritonitis is one of the most common complications of peritoneal dialysis (PD), which contributes to an increased number of hospitalizations of patients on PD (peritoneal dialysis) and failure which is the primary reason for leaving the continuous peritoneal dialysis (CAPD) and switch patients to hemodialysis. The most common bacterial causes of peritonitis in patients on peritoneal dialysis are gram-positive microorganisms. Coagulase-negative species of staphylococci were responsible for nearly half of all gram-positive episodes of peritonitis.

OBJECTIVE: To determine the frequency of isolated species of coagulase-negative staphylococci in dialysis effluent as the cause of peritonitis in CAPD patients.

MATERIALS and METHODS: The study included 37 patients on CAPD, treated at the Clinic of Nephrology, Clinical Center University of Sarajevo in a period of one year. Samples of dialysis effluent were taken for microbiological analysis every two months as well as urgently in case of emergency and symptoms of peritonitis. All samples were analyzed using standard microbiological methods.

RESULTS: A total of 162 samples of dialysis effluent were processed microbiologically. The negative samples were 82.7% and positive 17.9%, dominated by coagulase-negative staphylococci.

CONCLUSION: Peritonitis caused by coagulase-negative staphylococci remains the most common complication of CAPD. Identification and determination of antimicrobial susceptibility to targeted therapy make possible eradication of this cause of peritonitis.

Key Words: Peritonitis, peritoneal dialysis, coagulase-negative species, *Staphylococcus*



Evaluation of HBsAg, Anti-HCV, Anti-HIV1/2 and Syphilis Seroprevalence of the Blood Donors in Diyarbakir Region

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OBJECTIVE: The objective is to obtain the seroprevalence of HBsAg, anti-HCV, anti-HIV, RPR and to assess their rates according to time, gender in blood donors.

MATERIALS and METHODS: HBsAg, anti-HCV, anti-HIV and RPR results of 39.873 blood donors from September 1, 2007 to April 1, 2011 have been evaluated retrospectively. HBsAg, anti-HCV, anti-HIV and syphilis were examined by microparticle ELISA system.

RESULTS: 38.876 (97.5%) of the 39.873 donors were male and 997 (2.5%) were female. HBsAg was positive in 2.259 (5.66%), anti-HCV in 300 (0.75%), anti-HIV in 2 (0.00005%) of the donors. Syphilis was positive in 67 (0.0044%) of the 15.165 donors.

CONCLUSIONS: Seropositivity rate of HBsAg was higher than that of Turkey in general.

Key Words: Blood donors, HIV, HBV, HCV, syphilis



The Comparison of the Diagnostic Values of Rapid Urease Test and *Helicobacter pylori* Stool Antigen in Patients with Dyspeptic

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The prevalence of *Helicobacter pylori* infection which is the most common infection in the world is also very high in Turkey. These bacteria is acquired in early childhood and persists throughout life unless a treatment applied. *H. pylori* infection is the major cause of chronic gastritis and peptic ulcer disease in adult and children and it is a risk factor for the development of mucosa associated lymphoid tissue lymphoma and gastric carcinoma. Its diagnosis and treatment are important because of the inconvenience to people. The aim of this study was to compare the diagnostic accuracy of rapid urease test and *H. pylori* stool antigen (HpSA) in diagnosis of *H. pylori* infection in patients with dyspeptic complaints in our city.

One hundred and fifty three patients with dyspeptic complaints, who were admitted to endoscopy unit were included in this study, between January 2010 and March 2010. The routine gastrointestinal endoscopy, rapid urease test (CLOtest) and HpSA test was applied to these patients for evaluate *H. pylori* infection. The results of rapid urease test and HpSA test were compared.

A total of 153 patients, 73 were males and 80 were females. 102 patient's test results were negative, 51 of them were positive. Forty eight patients of male's rapid urease test and HpSA were negative, 22 of them were positive. Fifty four patients of female's rapid urease test and HpSA were negative, 29 of them were positive.

Key Words: Rapid urease test, HpSA, comparison



Comparison of Culture, BD ProbeTec ET and EZN for Detection of *Mycobacterium tuberculosis*

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INTRODUCTION: Mortality and morbidity due to mycobacterial infections are higher in developing countries. It is important to provide rapid and reliable detection of *M. tuberculosis* to prevent the spread of the disease. Although several methods can be used for the detection of *M. tuberculosis*, culture (Lowenstein-Jensen and MGIT) remains the gold standard. Because mycobacteria are slow-growing microorganisms, these tests take approximately 2-8 weeks. The length of conventional tests has led to new searches for rapid diagnosis in recent years. For this purpose, nucleic acid amplification (NAA)-based systems have been developed to show the presence of *M. tuberculosis* directly from the patient samples. In our study, it's aimed to compare the retrospective results of culture, EZN and BD ProbeTec ET.

MATERIALS and METHODS: The results of the samples with suspected tuberculosis that had been sent to the microbiology laboratory in Ondokuz Mayıs University Faculty of Medicine were analyzed retrospectively. Samples submitted to the laboratory were included in the process of decontamination. Then, 150 µL of the processed sample was inoculated onto Lowenstein-Jensen medium and incubated at 37°C for 4-8 weeks. Also, 0.5 mL of the same sample was inoculated into MGIT tubes and incubated in the Bactec MGIT 960 system. Smear was prepared from processed sample. Also, all samples were performed in the BD ProbeTec ET system with the steps of removing inhibitors, heating, extraction of DNA, neutralization and amplification according to the recommendations of the manufacturer.

RESULTS: A total of 703 samples with suspected tuberculosis that had been performed by three methods were evaluated. These materials include sputum (168), gastric fluid (131), urine (124) and other samples. The results of culture, EZN and BD ProbeTec ET are shown in Table 1.

Specificity, sensitivity, positive predictive and negative predictive values of the comparison of EZN and BD ProbeTec ET to culture are given in Table 2.

DISCUSSION: Early and reliable diagnosis is very important for the control of tuberculosis. Today, the easiest and fastest method in the diagnosis of tuberculosis is demonstration of acid-fast bacilli by Erlich Ziehl Nielsen (EZN) staining. However, 5000-10000 bacteria per mL are required for staining and smear microscopy. The gold standard for diagnosis of mycobacterial infections is the classical diagnostic culture method. But, new methods that can give rapid results are needed due to the length of culture period. As a conclusion, culture maintains its importance in the detection of tuberculosis bacilli, but we also suggest that BD ProbeTec ET is a reliable system that can give rapid results with high specificity and sensitivity.

Key Words: Lowenstein-Jensen, MGIT, BD ProbeTec ET EZN, *Mycobacterium tuberculosis*

Table 1. The results of culture, EZN and BD ProbeTec ET

		BD ProbeTec ET		EZN	
		Positive (42)	Negative (661)	Positive (26)	Negative (677)
Culture	Positive (39)	34	5	16	23
	Negative (664)	8	656	10	654

Table 2. Comparison of specificity, sensitivity, positive predictive and negative predictive values of EZN and BD ProbeTec ET

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
BD ProbeTec ET	87.1	98.7	80.9	99.2
EZN	41.0	98.4	61.5	96.6

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Risk Factors for Mortality in Patients with Nosocomial Gram-Negative Rod Bacteremia

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BACKGROUND: The percentage of hospital-acquired bloodstream infections associated with gram-negative bacilles has decreased during last decade but it is still a major cause of morbidity and mortality.

OBJECTIVE: The aim of this study was to determine the outcome of GNR bacteremia, which is an important clinical problem with high mortality rates, and the risk factors for GNR related mortality in our clinic.

MATERIALS and METHODS: During the study period, 520 episodes of bacteremia were detected in 411 patients. Only patients with GNR bacteremia in blood cultures were included in the study (n= 197). Among 197 patients fulfilling study criteria, GNR were grown in 239 samples.

RESULTS: *Escherichia coli* (n= 97, 40.5%), *Klebsiella pneumoniae* (n= 54, 22.5%), *Pseudomonas aeruginosa* (n= 24, 10%), *Acinetobacter baumannii* (n= 24, 10%) were the most commonly isolated bacteria. The most frequently identified infection sources of bacteremia were pneumonia (n= 35, 17.7%), catheter-related infection (n= 24, 12.2%), urinary tract infection (n= 20, 10%). In multivariate analysis, it was found that the GNR bacteremia mortality risk increased in patients treated in ICU (OR: 0.2, p= 0.03) and patients with ventilatory support (OR: 20.8, p= 0.05).

CONCLUSION: In clinical practice of the hospital settings, efforts should concentrate on preventive measures for nosocomial infections since pneumonia, catheter-related infections, and urinary infections appear to be the most frequent causes of secondary bacteremia.

Key Words: Bacteremia, mortality, nosocomial infection, risk factors

The Evaluation of Gram-Negative Microorganisms Caused Nosocomial Infections in Intensive Care Unit of a University Hospital

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INTRODUCTION: The aim of this study was to distribution of gram negative microorganisms caused nosocomial infections and evaluation of resistance status within 2010 year in intensive care unit (ICU) of an university hospital.

MATERIALS and METHODS: Between 1 January 2010 and 31 December 2010 based on the patient, active, prospective surveillance is made in ICU of Mustafa Kemal University Research Hospital. Centers for Disease Control and Prevention (CDC) diagnostic criteria were used for nosocomial infection diagnosis. Infectious agents isolated from patients in ICU were identified by conventional methods and VITEK2 Compact System (bioMérieux, France). According to the standards of Clinical and Laboratory Standards Institute (CLSI); antibiotics susceptibility tests were performed by using disc diffusion method.

RESULTS: During the study period 101 microorganisms were isolated from patients with nosocomial infection. 60.4% of 101 microorganisms were gram-negative microorganisms, 22.8% of them were gram-positive microorganisms and 16.8% were *Candida* spp. The distributions of gram-negative microorganisms were shown in Table 1. Extended spectrum beta-lactamases (ESBL) positive rates 52.6% were found in *Escherichia coli* strains. Antimicrobial drug resistances of gram-negative microorganisms were shown in Table 2.

CONCLUSION: Nosocomial infections caused gram-negative microorganisms were more common in ICU of our hospital. To know the ratio of antibiotic resistance against these agents will be guided to the empiric antibiotic treatment. High carbapenem resistance against *A. baumannii* is remarkable. High resistance ratio suggests that increasing of infection control preventions and revising the antibiotic usage politics must be required.

Key Words: Gram-negative bacterial infections, intensive care unit, nosocomial infection

Table 1. The distribution of gram-negative microorganisms

Microorganisms	%
<i>Acinetobacter baumannii</i>	50.8
<i>Escherichia coli</i>	31.2
<i>Pseudomonas aeruginosa</i>	16.4
<i>Stenotrophomonas maltophilia</i>	1.6

Table 2. Antimicrobial drug resistances of gram-negative microorganisms (%)

	<i>A. baumannii</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
Amikacin	47.8	0.0	66.7
Gentamicin	45.2	63.2	40.0
Piperacillin-tazobactam	92.9	27.8	55.6
Imipenem	83.9	0.0	40.0
Meropenem	80.7	0.0	50.0
Cefepime	93.3	83.3	50.0
Ceftazidime	92.3	87.5	44.4

Epidemiology of Nosocomial Infections Occurring in the Neurosurgery Intensive Care Unit of Dr. Lutfi Kirdar Kartal Training and Research Hospital

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OBJECTIVE: In this study, the epidemiology of nosocomial infections occurring in the neurology intensive care unit (NICU) was investigated.

METHOD: This study was performed at a secondary referral hospital between January 2007 and December 2010. Two hundred and one patients admitted to the NICU were examined retrospectively. Epidemiologic data for 65 cases with nosocomial infections were analyzed.

RESULTS: Two hundred and one patients were followed in the NICU for a mean period of 8.2 ± 7.9 days of stay; of these, 65 (32.4%) had a nosocomial infection. The mean age of these 65 cases was 47.5 (range: 1-92) years and the mean stay in the intensive care unit was 24.2 ± 10.3 days. Seventy-four (36.6%) patients followed in the NICU died while in intensive care and a nosocomial infection was found in 26 (36.1%) of these cases. Of the 91 culture samples taken from cases with a nosocomial infection, 43 (46.4%) had gram-positive organisms, 48 (52.5%) had gram-negative organisms, and one (1.1%) had *Candida* spp. The most frequently isolated gram-positive pathogen was methicillin-resistant *Staphylococcus aureus* (13.1%), and the most frequently isolated gram-negative pathogen was *Pseudomonas aeruginosa* (13.1%). The methicillin resistance rate among *Staphylococcus* strains was 57.1%. The imipenem resistance rate among *P. aeruginosa*, *Escherichia coli* and *Acinetobacter baumannii* strains was 66.4%, 25%, and 62.8%, respectively.

CONCLUSION: Knowledge of the epidemiology of the nosocomial infections that develop in the NICU will make an important contribution to both infection control and to decisions on the timing of the introduction of effective antibiotic regimens by physicians.

Key Words: Antibiotic resistance, neurosurgery intensive care unit, dangerous pathogens, intensive care infections, infection control

The Vancomycine and High Level Aminoglycoside Resistance of Enterococcus Isolated from Stools of Children with and without Diarrhea

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OBJECTIVES: Our aim is to investigate the colonization of enterococci in children's stool with and without diarrhea and the resistance of isolated enterococci to various antibiotics, especially vancomycine and high level aminoglycosides.

METHODS: We evaluated the enterococci strains isolated from the stool specimens of 379 children. Among them, 158 children had diarrhea and others were healthy. RapID STR (Remel) system was used for typing of strains. Only single strain from every stool specimen which resistant to one of vancomycine or streptomycine or gentamycine was included to the study. The resistance of every strain against ampicilline, erythromycin, tetracycline, rifampine and chloramphenicol was determined by Kirby-Bauer disc diffusion method in concordance with CLSI standarts. *vanA*, *vanB*, *vanC1* and *vanC2/3* genes were investigated by PCR in the 12 enterococcus strains resistant to vancomycine.

RESULTS: Among 379 enterococci, 12 (3.2%) were resistant to vancomycine (VRE), 38 (10%) were resistant to high level aminoglycosides (HLRA) and 7 (2%) were resistant to both of them. The rates of VRE and HLRA strains isolated from both diarrheal and healthy children's stool specimens showed no difference ($p=0.23$ and $p=0.27$). Two of the three vancomycine resistant *E. faecalis* strains isolated from diarrheal specimens had *vanA* gene and the other one had *vanC1* gene. Three of the four vancomycine resistant *E. casseliflavus* strains isolated from healthy children's stool specimens had *vanC1* and the other one had *vanC2/3* gene.

CONCLUSION: According to our results, healthy children's stool may also play an important role of transmission of VRE and HLRA enterococcus strains in Turkey.

Key Words: Diarrhoea, HLRA, VRE



Does Surgical Glove Perforation Increase Risk for Surgical Site Infection?

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OBJECTIVES: Glove perforation is a common problem during surgical procedures. The purpose of this study was to test the hypothesis that clinically visible surgical glove perforation is associated with an increased SSI risk.

METHODS: The data for this prospective observational study were collected in surgery clinics at Duzce University Hospital, in Turkey. The outcome of interest was SSI occurrence as assessed pursuant to the Centers for Disease Control and Prevention standards. The primary predictor variable was compromised asepsis due to glove perforation.

RESULTS: A total of 9 instances of SSI (3.9%) were detected in the 228 procedures studied. Culture specimens of whom obtained from four patients with SSI were negative. Two patients have polymicrobial growth in surgical site culture specimens. Organisms isolated from the surgical site specimens were *Pseudomonas aeruginosa* (n= 2), *Enterobacter* spp. (n=2), coagulase-negative staphylococci (n= 2), *Escherichia coli* (n= 1), *Klebsiella pneumoniae* (n= 1). Surgical glove perforations were occurred in 24.1% (55/228) of operations. In the absence of surgical glove perforation, the SSI rate was 3.5% (6/173). On the contrary, in the presence of surgical glove perforation, the rate of SSI was 5.5% (3/55). The rate of SSI was higher in surgical procedures in which gloves are perforated, but there was not a statistically significant difference (OR, 1.6; 95%CI, 0.4-6.6; p> 0.05).

CONCLUSION: The present study shows that surgical glove perforation may increase the risk for SSI. Efforts to decrease the frequency of glove perforation, such as double gloving and the routine changing of gloves during lengthy surgical procedures, are therefore encouraged.

Key Words: Surgical gloves, glove perforation, risk of surgical site infection



Incidence and Risk Factors of Nosocomial Pneumonia in Intensive Care Units

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INTRODUCTION: Nosocomial pneumonia (NP) is the most frequent nosocomial infection in intensive care units (ICUs). The evaluation of risk factors in patients with NP may provide useful guidance for patients who need intensive care.

MATERIALS and METHODS: A total 304 patients with nosocomial pneumonia in a tertiary medical center from May, 2006 to November, 2006 were prospectively followed. This study was conducted to determine risk factors and mortality of NP. During the six months period of time, patients who stayed in ICUs for at least 48 hours were included.

RESULTS: Among 304 patients, 78 (25.6%) had NP. The NP density rate was 23.1 per 1000 patient-days. Six variables were determined as independent risk factors for NP: advanced age (OR: 1; 95% CI: 1.001-1.059), length of stay in ICU (OR: 1.3; 95% CI: 1.166-1.393), prior infection on admission to ICU (OR: 6.7; 95% CI: 1.515-29.936), transfusion of blood and blood products (OR: 4; 95% CI: 1.425-11.462) and prior antibiotic usage within the last two weeks before admission (OR: 3.3; 95% CI: 1.283-8.475). As an additional risk factor, APACHE II score was significantly higher in patients with NP than in control group (p< 0.001).

DISCUSSION: The most important risk factors of NP in the ICUs were advanced age, length of stay in ICU, prior infection on admission to ICU, transfusion of blood and blood products, and prior antibiotic usage within the last two weeks before admission. High APACHE II score at nosocomial pneumonia onset was an independent and early predictor of mortality due to pneumonia.

Key Words: Nosocomial pneumonia, risk factor, intensive care unit



A Case of a Laboratory Acquired Brucellosis

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INTRODUCTION: Brucellosis is a zoonotic infectious disease and endemic in our country which is primarily transmitted by contaminated milk and milk products. *Brucella* can cause infections in laboratory workers through inhalation of aerosols and direct skin contact. *Brucella* spp. are among the most common bacterial infections which were gained in the laboratory conditions. In this paper, we reported a case of a laboratory acquired brucellosis infection.

CASE: A 26-year-old female patient who is a microbiology laboratory staff applied to our outpatient clinic with complaints of fever, fatigue, severe muscle and joint pain. In her anamnesis she said that she had injured her hand with contaminated syringe needle one month ago while she was working for blood culture of a patient in microbiology laboratory. It was learned after *Brucella* spp. bacteria reproduced in the related blood culture. Her brucella agglutination test was positive at 1/1280 titer and she was diagnosed as brucellosis. Rifampicin 600 mg/day and doxycycline 100 mg bid were commenced. She recovered without any complication after a total of 42 days treatment.

DISCUSSION: Brucellosis can be transmitted to health care staff via inhalation or direct contact in the laboratory. The most risky group is the microbiologists and technicians working in blood culture in the microbiology laboratory. Therefore, standard measures such as gloves and a mask applications for health staff are necessary and biosafety cabinets are required especially while working with bacteria. Clinicians must keep in mind that fever, muscle and joint pain are signs of brucellosis.

Key Words: Brucellosis, health staff



Detection and Identification of Toxigenic *Clostridium difficile* Strains in Antibiotic Associated Diarrhea

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C. difficile is an important pathogen in antibiotic-associated diarrhea. It is aimed to detect and identify toxigenic *C. difficile*.

Stool samples of 250 patients hospitalized and using antibiotics at last three weeks were examined macroscopically and microscopically. *C. difficile* toxin A-B was investigated by ELISA and positive samples were inoculated on cycloserine-cefoxitin fructose agar and incubated at 48 hours at 37°C on anaerobic conditions. Gram-positive bacilli producing terminal and subterminal spores was used for biochemical properties by API 20A panel.

Ten (4%) of 250 stool samples were found to be *C. difficile* toxin A-B positive. As a result of exposure to oxygen, growth was not seen in 4 of 10 strains of bacteria. The most frequently used antibiotics among toxin-positive patients were third generation cephalosporins. A variety of antibiotics such as meropenem, amikacin, teicoplanin, netilmicin and tigecycline were found to follow this.

Broad-spectrum antibiotics were commonly used in inappropriate manner in hospitalized patients. Tests that detect toxigenic *C. difficile* are required to take place among the routine diagnostic tests in clinical microbiology laboratories. The main way of reducing the rate of *C. difficile* associated diseases at hospitals is rational usage of antibiotics.

Key Words: *Clostridium difficile*, antibiotic associated diarrhea, toxin A-B



Lower Respiratory Tract Infection Rates Associated with Invasive and Non-Invasive Mechanical Ventilation in Patients with Respiratory Failure

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INTRODUCTION: Non-invasive mechanical ventilation (NIMV) may be a good alternative instead of invasive mechanical ventilation (IMV) in patients with respiratory failure.

AIM: To evaluate lower respiratory tract infections (LRTI) associated with IMV or NIMV in patients with respiratory failure treated in chest disease department.

METHOD: NIMV applied 182 and IMV applied 120 patients were evaluated retrospectively, between January 2005 and December 2006.

FINDINGS: The mean age of patients were 67.4 (± 11.4) and 67.9 (± 12.1) in groups applied NIMV and IMV respectively. NIMV group was composed of 131 (72%) of male and 51 (28%) of female whereas IMV group was composed of 69 (57.5%) of male and 51 (42.5%) of female. LRTI developed after 72 hours of mechanical ventilation at 24 cases in NIMV group (13%), whereas 30 cases in IMV group (25%). Four cases who developed LRTI associated with NIMV died and 11 cases who developed LRTI associated with IMV died. Meticillin resistant *Staphylococcus aureus* (n: 9/30, 30%) was the most frequent pathogen for LRTI in IMV group and *Acinetobacter baumannii* (n: 9/24, 38%) in the other group.

CONCLUSION: There was no significant difference between mortality rates of the groups. But LRTI rate was lower in NIMV group. Thus, in suitable cases in order to decrease LRTI, NIMV can be preferred instead of IMV.

Key Words: Invasive mechanical ventilation, noninvasive mechanical ventilation, lower respiratory tract infection

Surveillance of Invasive Device-Related Infection in a New Anesthesia Intensive Care and Reanimation Units for One Year

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Patients treated in Intensive care units (ICU) have increased risk of infection. Studies have shown that invasive equipment usage has brought the risk of invasive device-related infections (IDRI). We prospectively evaluated device utilization ratios, IDRI rates and causative agents according to active surveillance method based on patients and laboratory data in Rize Education and Training Hospital (400 beds), Anesthesia Intensive Care and Reanimation Unit (8 beds). During the one year-period of 2010, 290 patients were monitored for 2290 patient days. IDRI were identified according to the definitions of Centers for Disease Control and Prevention. A total of 17 IDRI were detected, the incidence was 7.4 per 1000 patient days. Ventilator-associated pneumonia (VAP, 94.0%, n= 16) was found to be the most frequent IDRI. Central venous catheter (CVC) related bloodstream infection (CVCRBI) rate was 6.0% (n= 1). No urinary catheter related infection (UCRI) was detected. Most frequently applied invasive device was found to be urinary catheter (100%). Mechanical ventilator usage was 66% and CVC application rate was 82%. The rate of VAP per 1000 device days was 10.57 and the rate of CVCRBI was 53%. The rate of IDRI and invasive device usage rates are shown in Table 1. Proper documentation of the first years' data of an ICU is important for preventing forthcoming nosocomial infections.

Key Words: Nosocomial infection, invasive device, intensive care unit

Table 1. The rate of invasive device related infections and invasive device usage

Infection	Invasive device	Device days	Rate of device usage (%)	Number of infections	Rate of infection (%)	Rate of infection per patient day
VAP	Mechanical ventilator	1514	66	16	94	10.5
CVCRBI	Central venous catheter	1884	82	1	6	0,53
UCRI	Urinary catheter	2289	100	-	-	-

VAP: Ventilator-associated pneumonia, CVCRBI: Central venous catheter related bloodstream infection, UCRI: Urinary catheter related infection.

One-Year Follow-Up Results of Tracheal Aspirate Culture and Antibiotic Resistance of Infectious Agents in a New Anesthesia Intensive Care Unit

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In this study, tracheal aspirate culture results in patients with mechanical ventilation in a new anesthesia intensive care and reanimation unit between January 2010 and January 2011, were retrospectively evaluated for pathogens and antibiotic resistance rates. A total of 33 patients, respective 94 tracheal aspirate samples and 657 test results were examined. Microorganismal growth has been detected in 88% of the samples (n= 77). The most frequently isolated gram-negative and positive pathogens were *Pseudomonas aeruginosa* (n= 26) and *Staphylococcus aureus* (n= 10), respectively. Other pathogens isolated were *Pseudomonas* spp. (n= 9), *Enterobacter* spp. (n= 2), *Acinetobacter* spp. (n= 8), *Escherichia coli* (n= 6), *Klebsiella pneumoniae* (n= 4), coagulase negative staphylococci (CNS) (n= 9), *Candida albicans* (n= 2), *Aspergillus* spp. (n= 1), respectively. *P. aeruginosa* species were found to have an antimicrobial resistance ratio of 52% for ciprofloxacin, 40% for gentamicin, 36% for imipenem and amikacin. *S. aureus* and CNS were found to have an antimicrobial resistance ratio of 100% for penicillin. Their antimicrobial resistance ratios for ciprofloxacin was found to be 44% and 60%, respectively. As a result, the most effective antibiotics against *P. aeruginosa* are found to be ceftazidime, cefoperazone, cefoperazone sulbactam and the most effective antibiotics are found to be glycopeptide and linezolid against gram-positive bacteria, carbapenem, third generation cephalosporins and amikacin against gram-negative bacteria in our intensive care unit. Possible pathogens and antibiotic resistance status should be carefully followed and recorded in intensive care units to provide good infection control measures.

Key Words: Antibiotic resistance, tracheal aspirate culture, intensive care unit

Table 1. Antibiotic resistance ratios of gram-negative microorganisms (%)

	<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas</i> spp.	<i>E. coli</i>	<i>Acinetobacter</i> spp.	<i>Klebsiella</i> spp.
Amicacine	36.0	25.0	0.0	12.0	0.0
Gentamicin	40.0	37.0	16.0	75.0	0.0
Meropenem	32.0	12.0	0.0	25.0	25.0
Imipenem	36.0	12.0	0.0	25.0	25.0
Ceftazidime	10.0	37.0	16.0	100.0	-
Ceftriaxone	20.0	37.0	33.0	37.0	0.0
Cefoperazone	15.0	25.0	-	-	-
Cefoperazon-sulbactam	15.0	26.0	-	-	-
Piperacillin	-	-	-	37.0	-
Piperacillin-tazobactam	32.0	50.0	25.0	37.0	-
Ciprofloxacin	52.0	56.0	66.0	87.0	0.0
TMP-SMX	-	-	66.0	88.0	0.0
Ampicillin	-	-	100.0	-	75.0
Amoxicillin clavulanate	-	-	33.0	-	-

TMP-SMX: Trimethoprim/sulfamethoxazole.

Table 2. Antibiotic resistance ratios of gram-positive microorganisms (%)

	CNS	<i>S. aureus</i>
Vancomisin	0.0	0.0
Penicillin	100.0	100.0
Erythromycin	75.0	50.0
Gentamicin	15.0	10.0
TMP-SMX	27.0	10.0
Ciprofloxacin	44.0	60.0
Linezolid	-	0.0
Tetracycline	33.0	20.0

CNS: Coagulase negative staphylococci (CNS),

TMP-SMX: Trimethoprim/sulfamethoxazole.



Occupational Exposure to Blood and Body Fluid Among Health Care Workers in a Teaching Hospital in Istanbul, Turkey

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Health care workers (HCW) are at an increased risk of exposure to blood and body fluids in their workplace. The objective of this study was to estimate the incidence of exposure to blood and body fluid among HCW. This was cross-sectional study among doctors, nursing staff, nursing students, support staff, technicians working in various clinical departments of Haydarpasa Numune Training and Research Hospital in Istanbul in the month of December 2010. A total 300 HCW participated in this study. The average age of respondents was 30.3 ± 7.2 (16-53). The study population included 41.6% nurses, 32% doctors, 12% support staff, 7.7% nursing student and 6.7% lab technicians. The incidence of exposure to blood and body fluids was 58.3%. The average number of exposure to blood and body fluids was found to be 2.5 per HCW (range, 0-10). Within the last year, exposure to potential infectious material occurred 45 (25.7%) of HCW. Both exposure to potential infectious material (50.9%) and self reported incidence (50%) were highest among the nursing staff. The most common mode of exposure was needle-stick injury (82.2% of total exposures). Highest rate of occupational exposure was seen in emergency department ($p= 0.043$), surgery clinics ($p= 0.045$) and lowest rate was observed in internal medicine clinics ($p= 0.017$).

Key Words: Health care workers, occupational exposure

Evaluation of the Microbial Contamination of Mobile Phones Used by Health-Care Workers

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OBJECTIVE: To evaluate the microbial contamination of mobile phones used by the health-care workers in a secondary referral hospital.

METHOD: This study was performed in all departments of Elazig Education and Research Hospital in July 2010. A total of 183 mobile phones are included into the study. Microbiologic cultures were taken from the mobile phones of all health-care workers, including nurses, laboratory workers, and health-care staff, using a sterile swab, and incubated in the liquid agar at 37.5°C for 24 hours. Thereafter, 5% sheep blood agar and EMB agar medium were used to grow the microorganisms. Sceptor microdilution system was used for the identification and antibiogram of microorganisms. This study was conducted in either day of week at about three o'clock PM without the noticing of health-care workers. Health-care workers who do not want to participate to the study were not included into the study.

RESULTS: A total of 183 mobile phone cultures of all health-care workers, of which 94 (51.4%) from the nurses, 32 (17.5%) from the laboratory workers, and 57 (31.1%) from the health-care staff, were evaluated in the study. Of these 179 (97.8%) were culture positive. The microorganisms isolated from the culture-positive specimens of mobile phones are shown in Table 1.

CONCLUSION: Mobile phones are important devices transmitting the dangerous pathogens between health-care workers and population-based community. The usage of these devices among health-care workers should be limited in hospitals.

Key Words: Mobile phones, health-care workers, health-care infections, dangerous pathogens, population-based community

Table 1. The microorganisms isolated from the culture-positive specimens of mobile phones

Health-care workers	<i>Staphylococcus</i> spp. n (%)	MRSA n (%)	GNB n (%)	ESBL (+) n (%)	Others n (%)
Nurses	12 (6.7)	6 (3.4)	18 (10.1)	11 (6.1)	57 (31.8)
Laboratory workers	12 (6.7)	5 (2.8)	6 (3.4)	2 (1.1)	13 (7.3)
Health-care staff	19 (10.6)	6 (3.4)	13 (7.3)	7 (3.9)	23 (12.8)
Total	42 (23.5)	17 (9.5)	37 (20.7)	20 (11.2)	100 (55.9)

MRSA: Methicillin-resistant *Staphylococcus aureus*, GNB: Gram-negative bacilli, ESBL(+): Extended-spectrum beta-lactamase positive, Others: Coagulase-negative *Staphylococcus* spp., *Enterococcus* spp., *Klebsiella* spp.



Possible Tuberculosis Transmission to Out Patients at Clinics and Recommendations

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Airborne transmitted tuberculosis disease may be frequently encountered in health workers, patients and visitors at hospitals. Poor and/or improper ventilation systems, delayed diagnosis to the source cases, actual immune conditions of the exposed person which may facilitate tuberculosis transmission may increase the risk or transmission. Visiting frequency and the ratio of tuberculosis development of the out-patients who refer to hospital for the diagnosis of chronic obstructive pulmonary disease (COPD) due to their frequent and regular visits to the hospital in February-December 2007 were studied at the health institution entitled the hospital of chest diseases and possible nosocomial tuberculosis cases probable to have developed at hospital visits were researched and the incidence was found to be 749/100.000, which is about 29 times the tuberculosis incidence nation-wide (26/100.000). This difference is calculated as significant ($p < 0.05$).

Key Words: Isolation cautions, tuberculosis, airborne transmitted diseases

Table 1. Clinic visits frequently

Clinic visits	COPD	COPD + TBC	%	1/100.000
0-5	986	8	0.81	
5-10	70	0	0	
10-15	5	0	0	
15↑	7	0	0	
TOTAL	1068	8	0.75	749

1068 patients visited the hospital of chest diseases and tuberculosis with COPD diagnosis in February-December 2007, who visited the hospital clinic for an average of 6 ± 4.8 (1-31) times. Frequency of clinic visit was classified as (0-5), (5-10), (10-15), (15↑). However, there was no relation found between the frequency of visits and tuberculosis transmission ($p > 0.05$).

Table 2. Average of patient admission and final diagnosis periods

Random 30 patients	Random 30 COPD diagnosed patients	
Avr. 58.8 min	Avr. 72.9 min	$p < 0.05$

In order to calculate patient admission and final diagnosis time of the clinic, 30 patients are selected randomly and such time is calculated as approximately 58.33 minutes over the automation system of our hospital. Such finding is compared with the period of time (72.9 min) in which 30 randomly-selected COPD diagnosed patients benefitted from clinical services ($p < 0.05$) (Table 3). However; as these parameters could not be observed for the hospital automation system in 2007, clinical waiting period of 8 patients could not be calculated. However, we can state with these findings that COPD diagnosed patients spent more time in the waiting room. As the reasons for such long waiting periods are examined, it is found that the longest waiting periods took place within 08.00-08.30 in the morning (with an average waiting period of 142.3 min) and the shortest waiting periods took place within 10.15-11.00 (with an average waiting period of 33 min).

Table 3. Demographical information

Average age	68.7 ± 15.8 (31-88)	
Female	1	12.5%
Male	7	87.5%
Prednol use (20 mg/G ↑)	2	25%
Cronic renal failure	0	0
Congestive heart failure	0	0
Tuberculosis history	1	12.5%
Pulmonary tuberculosis	7	87.5%
Tuberculosis pleuritis	1	12.5%
Types of diagnosis		
Clinical	8	100%
Radiological	8	100%
Pathological	1	12.5%
Microbiological	8	100%

In the same period, 8 potentially hospital-borne tuberculosis cases were identified following their last visit after an average of 35.3 ± 4.7 -day-long incubation. In ratio, the incidence is 749/100.000, which is about 29 times the nation-wide tuberculosis incidence (26/100.000). Such difference is evaluated as statistically different ($p < 0.05$).



The Investigation of Percutaneous Injuries Among Healthcare Workers at a State Hospital

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OBJECTIVE: Health care personnels are at risk for transmission blood-borne pathogens via percutaneous exposure. Of the 35 million health-care workers worldwide, 3 million experience percutaneous exposure to blood pathogens each year. The aim of this study was to assess of percutaneous injuries (PI), required precautions, and applications after the injuries among healthcare workers in a state hospital.

METHOD: Follow-up forms of PI reported to the committee of infection control in the state hospital were investigated retrospectively. A total of 36 cases of PI reported between January 2007 and November 2010 were assessed.

RESULTS: Of 275 health staffs, 36 personnel (13%) were exposed to, 44% of which were observed in nurses, 22% in doctors, and 34% in cleaning staffs. The device to damage most frequently was the needle-channel. The body part most likely to be involved were fingers. Ten sources were detected positive for HBV, four for HCV, and two for CCHFV. As a result of appropriate post-exposure prophylaxis and follow-up, none of these injured staffs were detected positive for any of the above mentioned infections.

CONCLUSION: Since most of the sources were infected, it was shown that the health personnel is endangered for infections PI. In addition, PI are often not reported. Reporting of PI is important for instigation of adequate post-exposure prophylaxis and follow-up. The health personnel should presume that all patients are infected, and thus should work following universal precautions to avoid complications about the PI.

Key Words: Health personnel, percutaneous injuries



Nosocomial Infections in a District Hospital

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MATERIALS and METHODS: The surveillance data of nosocomial infections in Kiziltepe General Hospital, 79-bed capacity, between 1 January 2010 and 31 December 2010, was evaluated. The epidemiological data was collected by laboratory and hospital-based active surveillance method.

RESULTS: 10.410 patients were hospitalized during this period. 27 (0.26%) hospital-acquired infections were detected. Incidence density was calculated to be 1.46. The highest rate of hospital infections (0.50%) was seen in the intensive care unit. The highest rate of infection was observed in the breast surgery clinic (4.1%). In total, 55.5% of detected hospital-acquired infections were surgical site infections, 25.9% urinary tract infections and 11.1% were pneumonia.

CONCLUSION: The low infection rate was related with rapid patient circulation.

Key Words: Nosocomial infections, surveillance, infection rate



Features the Epidemic Process of Influenza in Kazakhstan, 1990-2009

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In the Kazakhstan every year registered more than 1 million cases of influenza and influenza-like illness, not including those for medical attention for various reasons did not apply. In 2009 recorded 17 imported cases of influenza caused by virus type A H1N1 (swine like).

Influenza epidemic caused by serotype (H3N2) were more frequent (1990, 1992, 1996, 1999, 2000, 2003, 2004). Serotype virus AH1 caused the influenza epidemic in 1991, 1994, 1998, 2001, 2005 and 2009. The influenza epidemic of mixed etiology was observed in 1991, 1997, 2002 and 2006.

Epidemics of influenza type B-in 1993, 1995, 2007, 2008.

Morbidity caused by influenza A (H3) in 1990, 1992, 1996, 1999, 2000, 2002, 2004, 2006 shows a distinct tendency to become more frequent occurrence of influenza outbreaks. The incidence in the age groups 0-2 years ranged from 3.5 - 26.4%, 3-6 years 6.5-28.2%, 7-14 years 7.1-31.7%.

The proportion of influenza in the total incidence of influenza and ARVI ranged from 5.2% to 19.3%.

Results of virological, serological studies confirm the frequency and effectiveness of epidemic outbreaks of influenza caused by viruses A (H1N1), A (H3N2) and B. In season 2009-2010 solved etiology of 17 cases of influenza A "swine like".

Thus, we can note an intensification of the epidemic process of influenza in until 2009, both the frequency of recurrence, as well as to increase the incidence of influenza at the expense of children.

Thus until 2009 epidemiological process of influenza B different repetition and a high proportion of children.

Key Words: Influenza, virus, epidemic, virological



Investigation of the Effectiveness of the Environment and Surface Disinfectant "Fumispore OPP"

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INTRODUCTION and OBJECTIVES: Environmental contamination plays an important role for the transmission of nosocomial pathogens. Reduction of environmental contamination contributes to the control of nosocomial infections. "Fumispore OPP" contains 20% ortho-phenylphenol and makes disinfection through smoke from aerial. The aim of this study is to investigate antibacterial and antifungal effectiveness of "Fumispore OPP" in hospital environment and various surfaces.

MATERIALS and METHODS: The study was performed in three Hospital units (Operating Room, Burn Unit and Microbiology Laboratory) of Dicle University. Ambient air samples were collected just before the application of Fumispore OPP and after three hours later the application. The samples were collected by "Air Test Omega" air sampling device and surface samples using Thioglikolat Broth impregnated cotton swabs. Air samples were directly inoculated on blood agar (BPA) and Saboraud Dextrose Agar (SDA) media; swab samples were inoculated by spreading. Total Aerobic Colony Count (TACC) was determined using the standard method based on quantitative measurement of bacteria.

RESULTS: In this study, the TACC's mean values which were detected in ambient air respectively; 258 CFU/m³ for bacteria and 208 CFU/m³ for fungus before application, 20 CFU/m³ for bacteria and 15 CFU/m³ for fungus after application and were determined on surfaces respectively; 12.1 CFU/cm² for bacteria and 2.9 CFU/cm² for fungus before application, 1.6 CFU/cm² for bacteria and 0.36 CFU/cm² for fungus after application.

CONCLUSION: The detected values before and after the application have showed that this disinfectant is suitable for adequate disinfection.

Key Words: Disinfectant, fumispore OPP, total aerobic colony count (TACC)



Effect of a Influenza Epidemic in the Infant Mortality Rate in the Turkestan Region South Kazakhstan Oblast, Kazakhstan

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Influenza rarely causes death but the great role of its complications, the additional morbidity and mortality population in the epidemic and the subsequent periods.

We analyzed infant mortality among inhabitants of Turkestan region of South Kazakhstan oblast against infectious diseases, particularly influenza.

The analysis was performed on the basis of the official registration of morbidity, infant mortality rates against the overall mortality rate from different causes.

The 17-year period (1993-2009) in the Turkestan region, the epidemic process of influenza have been characterized by intermittent flow: for 6 years, various cases of influenza have not registered, high epidemic was 1997, 2001, 2003 years.

The high incidence of influenza, was registered in 2003 (237.6 per 100.000 population), exceeded of long standing the average in 7.8 times more.

Among the causes of infant mortality are equally important as social and medical factors, and infectious (especially viral) pathology maternal, fetal and postnatal infant infection.

We separately analyzed infant mortality rates for two periods: the years 1993-1999 with the most severe medical and social conditions and 2000-2009 with a real improvement in the socio-economic indicators of living standards.

During the first period the average annual infant mortality rate was 23.5 ± 1.06 and for the second -16.3 ± 0.94 per 1000 live births, the difference was equal to 5.1 for a tabular -2.16 .

The significance of differences between the compared periods of very high $p < 0.01$.

Consequently, improving the quality and quantity of medico-social care is one of the leading factors of lowering infant mortality.

Key Words: Influenza, infant mortality, medico-social care

Molecular Microbiology

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Molecular Characterization of *Salmonella* Serotype *Typhimurium* Strains Isolated in Turkey by Plasmid Profiles and Pulsed Field Gel Electrophoresis

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OBJECTIVES: Our aim is to investigate the molecular characteristics of *Salmonella* serotype *Typhimurium* strains isolated in Turkey by plasmid profile and pulsed field gel electrophoresis (PFGE) patterns.

METHODS: A total of 113 *S. Typhimurium* strains which had been isolated from clinical samples, serotyped and tested for antimicrobial susceptibility using agar dilution method in the previous study were selected from the culture collection of Enterobacteria Laboratory of our department. Out of the selected strains only 24 isolates (21.23%) were susceptible to all antimicrobials tested whereas 73 (64.6%) isolates were multidrug resistant (MDR). Molecular characterizations of the isolates are investigated by plasmid profile analysis and PFGE methods.

RESULTS: One hundred (88.49%) isolates harboured one to three plasmids ranging in sizes from 1.0 to 180 kbp. The 75.2% of the whole strains and 56.16% of the MDR isolates carried the 90 kbp sized plasmid alone or together with other plasmids. PFGE performed with restriction enzymes *XbaI* and *SpeI*, the isolates were grouped into 20 profiles with both restriction enzymes. Cluster analyses based on PFGE, 80 of the 113 (70.8%) isolates with *XbaI* and 79 of the 113 (69.91%) isolates with *SpeI* were grouped into one profile (X15 and S17 respectively). Combination of *XbaI* and *SpeI* profiles gave a total of 30 profiles, 75 (66.4%) of the 113 isolates belonging to X15/S17 profile. Out of those 75 strains, 64 of them (85.3%) were MDR.

CONCLUSION: These results showed that the most common isolated *S. Typhimurium* human strains in Turkey had genetically similar characteristics.

Key Words: PFGE, plasmid profiles, *Salmonella* serotype *Typhimurium*, Turkey



Class 1 Integrons in Multidrug Resistant *Salmonella enterica* Serovar *Typhimurium* Isolated in Turkey

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OBJECTIVES: Multidrug resistance in bacterial pathogens including *Salmonella* is now a common phenomenon worldwide. Integrons are a major vehicle for the spread of multiple-antibiotic resistance. In this study, 66 sporadic, multidrug-resistant (MDR) isolates of *Salmonella enterica* serovar *Typhimurium* (resistant to at least four unrelated antimicrobial agents) collected in Turkey (2000-2002) were screened for carriage of class 1 integron and plasmid.

METHODS: A total of 66 MDR (isolates of R-type AA/CCSSuT) *S. Typhimurium* strains which had been tested for antimicrobial susceptibility using agar dilution method in the previous study were selected from the culture collection of Enterobacteria Laboratory of our department. The presence of integrons was investigated by PCR using specific 5'CS/3'CS primer pair. All isolates were also analyzed for the presence of plasmids.

RESULTS: Among the isolates 65.2% contained class 1 integrons. PCR amplification of class 1 integrons showed five diverse bands of approximately 350 and 1600 kbp. All of the isolates harboured one to four plasmids ranging in sizes from 1.0 to 180 kbp. The plasmid sized 90 kbp was the most common plasmid, 92.4% of the isolates carried 90 kbp plasmid alone or together with other plasmids.

CONCLUSION: The strains carried 65.2% and 100% of class 1 integrons and plasmids respectively, which may explain the dissemination of antimicrobial resistance genes through these elements. Our findings show that integrons are widely disseminated among MDR *S. Typhimurium* strains from clinical samples in Turkey, thereby suggesting their importance in conferring this resistance profile.

Key Words: Integron, plasmid, *Salmonella Typhimurium*



A Pilot Study for Screening Blood Donors by Nucleic Acid Amplification Technology in Turkey

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OBJECTIVE: Blood donors in Turkey currently are screened for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus infection by immunoassay. The risk of enzyme immunoassay (EIA)-negative, nucleic acid amplification technology (NAT)-reactive donations is not well understood. This study aimed to screen for such donors in Turkey by a multiplex test on a commercially available NAT system.

MATERIALS and METHODS: NAT was performed on donors without prescreening in pools of six and NAT-reactive pools were then resolved to the single donation. Individual-donor NAT-reactive samples were discriminated by a commercially available polymerase chain reaction (PCR)-based diagnostic assay (COBAS AmpliScreen, Roche). Samples with EIA- and NAT-discordant results were investigated with supplemental serologic and confirmatory tests. Each sample taken from follow-up of HBV NAT yield cases was tested for HBV serologic profile, NAT, and viral load.

RESULTS: Among 3000 seronegative donations, 9 HBV NAT yield cases (0.3%) and 1 HCV (0.03%) and 1 HIVNAT yield case (0.033%) were detected. Follow-up results showed that the HCV yield case was a window period and all HBV NAT yield cases were occult carriers.

CONCLUSION: The use of NAT detected occult HBV and reduced HCV window period. The yield rate, especially occult HBV, was higher than that in developed, nonendemic countries. Therefore, NAT implementation for routine donor screening in a more cost-effective manner should contribute to safer blood transfusion in Turkey.

Key Words: Blood donor, HCV, HBV, HIV, NAT



Epidemiological Analysis of *Salmonella enterica* Isolated from Food in Morocco

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Non-typhoidal *Salmonella* (NTS) cause foodborne disease worldwide especially in developing countries. Molecular characterization is an important tool to control the spread of this pathogen. In this study, 102 *Salmonella enterica* of 15 different serovars, isolated from food samples in Morocco, were analysed by antimicrobial testing, macrorestriction profiling by PFGE, plasmid profiling and genetic determinants of resistance. PFGE revealed one main *Xba*I pulsotype and from 2 to 5 sub-profiles for each serovar, with a total of 38 different genotypes. Thirty-six percent of the strains carried from 1 to 4 plasmid with a total of 12 different profiles. Twenty-six percent of *Salmonella* isolates displayed resistance to at least one antimicrobial and ampicillin and nalidixic acid resistance were recorded respectively in 13% and 3.8% of the isolates. Multiple resistance (MDR) was observed in five *S. Typhimurium* DT104 and in two *S. hadar* isolates. MDR in *S. Typhimurium* DT104 was associated to intact *Salmonella* genomic island 1. In *S. hadar* isolates resistance to ampicillin and nalidixic acid was due respectively to *bla*TEM1 gene and a mutation in both *gyrA* (*Asp87Asn*) and in *parC* (*Thr57Ser*) genes. The findings of this study highlight the importance of monitoring *Salmonella* isolates to avoid the spread of MDR strains.

Key Words: *Salmonella*, antibiotic resistance, PFGE



Molecular Analysis of Carbapenem Resistance and Identification of Clonal Relationship Among Nosocomial *Acinetobacter* Strains from Turkey

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The aim of this study is to determine drug susceptibility patterns of *Acinetobacter* isolates which cause hospital infections, and OXA type beta lactamases enzymes distribution which is the main cause of carbapenem resistance in clinical isolates of multidrug resistant *Acinetobacter* strains, and besides the clonal relationship between isolates by Arbitrarily Primed PCR method. All strains were found to be susceptible to colistin. When the resistant rates of other 13 antibiotics were compared, it is found that netilmicin had the lowest resistant rate (44%) and ciproflaxacin had the highest resistant rate (99%). The resistant rates of imipenem and meropenem were found as 84% and 96%, respectively.

blaOXA-23 genes were examined with PCR method and *blaOXA-51* gene specified to *Acinetobacter baumannii* was found positive in 99% of all strains. The ratio of *blaOXA-23*-like gene and *blaOXA-58* gene in carbapenem resistant strains was determined as 75% and 23%, respectively. At least one of the *blaOXA-23*-like and *blaOXA-58* gene was found in 90% of all strains.

With the clonal analysis of *Acinetobacter* strains causing hospital infections by using AP-PCR method, two main clons were determined and named as A and B. It is figured out that B1 (the subtype of B clon) is still found in internal medicine intensive care unit as potential hospital infections.

In this study, high prevalence of OXA type carbapenemases and high resistance rates to beta-lactamases antibiotics were noticeable and it is observed that AP-PCR method was successful to show the clonal relationship in epidemic analysis caused by hospital infections.

Key Words: *Acinetobacter* spp., carbapenem resistance, OXA-type carbapenemases, AP-PCR



Molecular Characterization of CTX-M β -Lactamase Producing *Escherichia coli* from Turkey

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This study aimed to examine the type of CTX-M group enzymes in ESBL producing *E. coli* isolated from clinical samples.

A total of 280 clinical isolates were collected from patients from January 2003 to May 2008. Of the 280 strains, 113 were nosocomial and 167 were community acquired isolates were from; urinary tract specimens (214), the respiratory tract (23), catheter (4), blood (4), and other types of specimen (35). All isolates were identified by conventional methods and ESBL production was detected by double-disc synergy tests interpreted according to Clinical and Laboratory Standards Institute (CLSI) criteria.

The presence of *bla*CTX-M gene was screened by PCR using universal primers; CTX-M.F 5'-TTTGCGATGTGCAGTAC-CAGTAA-3' and CTX-M.R 5'-CGATATCGTTGGTGGTGCCATA-3'.

Amplified 544-bp internal fragments of *bla*CTX-M genes were directly sequenced using the primers CTX-M.F' and CTX-M.R' on the ABI PRISM 310 Genetic Analyzer (Applied Biosystems, ABD).

Among the 280 strains, all tested were susceptible to imipenem and resistant to ampicillin. Resistance of ESBL isolates to other antibiotics was cephalothin (89.0%), amoxicillin/clavulanic acid (79.7%), ciprofloxacin (71.1%), trimethoprim-sulfamethoxazole (67.3%), aztreonam (65.2%), ceftriaxone (62.2%), gentamicin (42.0%), cefepime (36.5%), ceftazidime (26.8%), piperacillin-tazobactam (5.0%).

The CTX-M-type beta-lactamase genes were detected in 205 of 280 (73.2%) ESBL producers. Overall *bla*CTX-M-15 was the commonest genotype (89.2%) followed by *bla*CTX-M-1, (6.8%) *bla*CTX-M-3 (3.4%), and *bla*CTX-M-33 (0.4%). CTX-M producer strains were prevalent among community-acquired infections (64.8%) Most of all CTX-M-bearing isolates (98.5%) were from urine specimens. Multidrug-resistant CTX-M-15-producing *E. coli* is emerging worldwide as an important pathogen causing community-onset and hospital-acquired infections.

Key Words: CTX-M group enzymes, β -lactamase, *E. coli*, antimicrobial resistance

Francisella tularensis Subspecies *holarctica* Isolates from Turkey Lack Bacterioferritin: Does This a Clue for Virulence?

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Francisella tularensis is the causative agent of tularemia. In this study, we investigated the protein composition of the *F. tularensis* subsp. *holarctica* strains using a comparative proteomic analysis.

Eight strains from different locations in Turkey and a standard *F. tularensis* subsp. *holarctica* NCTC 10857 were grown at 37°C on cystine heart agar with sheep blood (CHAB). Cells were resuspended in the lysis buffer and, exposed to freeze thaw cycles before sonication. A total of 80 µg protein was loaded onto each IPG (pH 5-8) strip and were focused on Protean IEF cell. After SDS-PAGE, all images were analyzed with PDQuest Advance (BioRad, USA). Eleven up or down regulated major spots were identified by MALDI-TOF/TOF (Applied Biomics, USA).

Analysis of proteom profiles of all isolates indicated that unlike the standard strain, Turkish isolates do not possess bacterioferritin, an iron storage protein. This cannot be linked to culture conditions since all of the studied strains were cultured in CHAB medium containing the same amount of iron. In the literature, higher levels of bacterioferritin have been reported in LVS and other subsp. *holarctica* strains relative to *F. tularensis* subsp. *tularensis*.

Several lines of data implies the involvement of iron in the virulence of *F. tularensis*. Our finding of the fact that Turkish strains cause much less severe disease and at the same time lack bacterioferritin, strengthens the possibility of the link between bacterioferritin and virulence. Further work utilizing shuttle vectors and creating bacterioferritin knock-out strains are needed to assure the effect of bacterioferritin on virulence.

Key Words: *Francisella tularensis*, bacterioferritin, proteom analysis

Strain 3

F. tularensis subsp. *holarctica* NCTC 10857

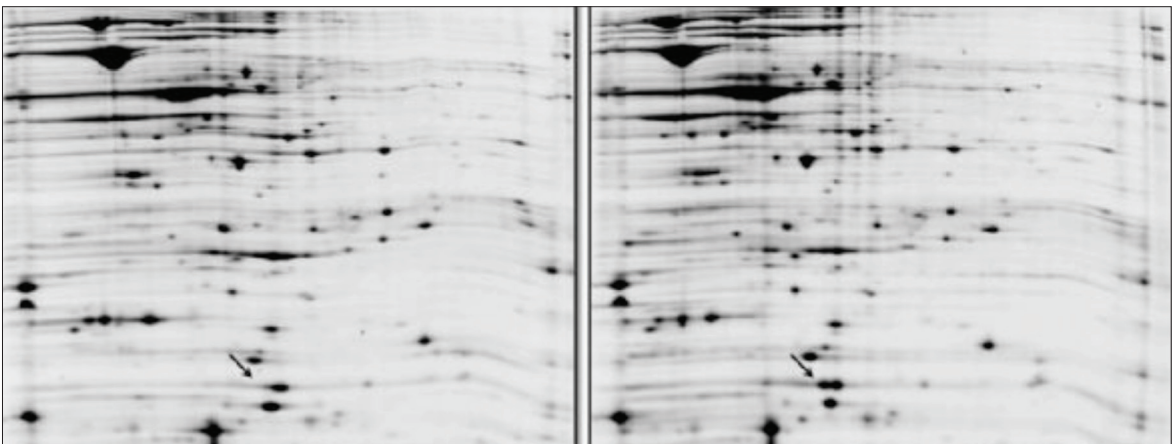


Figure 1. Representation of comparative proteome analysis of a strain of Turkish isolate with *F. tularensis* subsp. *holarctica* NCTC 10857.



Hidden Spread of *bla*OXA-48 Gene Among the ESBL Producing *Escherichia coli* and *Klebsiella pneumoniae* Isolates in Pediatric Intensive Care Unit

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PURPOSE: The concern is increasing that the *bla*OXA-48 producing strains may be hidden spreading due to the detection of this kind of strains as susceptible with routine laboratory methods. The purpose of the study was to detect *bla*OXA-48 gene among the ESBL producing *K. pneumoniae* and *Escherichia coli* isolates.

MATERIALS and METHODS: Ninety-two ESBL producing isolates (*Escherichia coli*: 66, *K. pneumoniae*: 26) were included from 2010. The antibiotic susceptibility test was performed using the disc diffusion method and VITEK 2 system. Carbapenemase activity was screened by the Modify Hodge test. Beta-lactamase genes were detected by PCR and *bla*OXA-48-positive ones were sequenced. Genetic relatedness between *K. pneumoniae* isolates were investigated by PFGE.

RESULTS: All 92 strains were found to be susceptible to imipenem and meropenem with disc diffusion method. Carbapenemase activity is detected in 10 isolates (One *E. coli*, nine *K. pneumoniae*) by Modify Hodge test. *Bla*OXA-48 genes in these isolates were demonstrated by PCR and sequence analysis. All ten isolates were found to be susceptible to imipenem, meropenem but one *E. coli* and five *K. pneumoniae* isolates were resistant to ertapenem (MIC \geq 8). Additionally, nine isolates co-produced at least one beta-lactamase including SHV, CTX-M or VEB-1 type. PFGE revealed different pulso-types among nine *K. pneumoniae* isolates.

CONCLUSIONS: OXA-48-producing isolates may be found in the susceptible range to carbapenems according to CLSI guidelines. Ertapenem seems to be a better indicator for their detection due to hydrolyzing effect of these enzymes. The dissemination of *bla*OXA-48 gene is not spread by a single *K. pneumoniae* clone, several OXA-48-producing clones were distributed in Istanbul.

Key Words: Carbapenemase, OXA-48, VEB, antibiotic resistance, ESBL



Multiplex PCR Assay for Identification of Some Pathogenic Bacteria

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Bacterial pathogens are increasingly important concern in many part of the world. Identification of four different pathogens species from biological materials was carried out using PCR techniques. PCR assay was performed using species definite primer set. Four different primer pairs were used to identify *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli* and *Pseudomonas aeruginosa* species. Primers were designed to amplified 400, 407, 254 and 249 bp long fragments using *mecA*, *spy1258*, *aggR* and *oprI* genes respectively. Two different multiplex PCR reactions were planned. In reaction I, *S. aureus* and *E. coli* isolates were identified and *S. pyogenes* and *P. aeruginosa* isolates were confirmed using reaction II. PCR amplification was performed in a 40 μ L reaction volume and bacterial colony was used as template DNA. Both Reaction I and Reaction II thermal cycling parameters were as follows: 94°C for 5 min; followed by 30 cycles of 94°C for 30 s, 60°C for 30s, 72°C for 1 min; and a terminal extension step of 72 for 10 min. The multiplex PCR presented here is a rapid diagnostic tool for identification of different pathogens using designed primers.

Key Words: Multiplex PCR, identification, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*.



Evaluation of the Association of *cagA* 3' Polymorphisms and Candidate Virulence Genes Encoding Glycosyltransferases and Outer Membrane Proteins with Clinical Outcome in Turkish *Helicobacter pylori* Isolates

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Clinical severity in *Helicobacter pylori* infections seems to depend on a number of factors including differences in *H. pylori* virulence, host genetic susceptibility and environmental factors. Putative *H. pylori* virulence factors associated with an increased risk of a clinical outcome include *cag PAI*, *jhp0562* gene, encoding a glycosyltransferase involved in the synthesis of the lipopolysaccharide, *homB* gene related to *H. pylori* outer-membrane proteins.

The aim of this study is to evaluate the association of *cagA* 3' polymorphisms and, *jhp0562* and *homB* presence and the effect of these genes to the clinical relevance.

H. pylori strains were isolated from gastric biopsy samples of 42 adult patients. DNA extraction from bacterial cultures was performed by using spin column DNA extraction kit. Oligonucleotide primers directed to consensus regions of *cagA* 3', *jhp0562* and *jhp0563* like genes and *homB* were used for the amplification. *cagA* (+) strains were analyzed by DNA sequencing for the polymorphisms. Histopathologic evaluation of gastric biopsy samples was done according to Sydney classification.

Twenty eight out of 42 strains were found to have *cag PAI* region (66.66%). In these strains polymorphisms due to insertion and deletion were detected. Twelve out of 42 strains were found to have *jhp0562* gene region (28.57%). Thirty out of 42 strains were found to have *homB* gene region (71.42%). Fourteen out of 42 strains were found to have *cag PAI* and *homB* gene region (33.33%) together. Sixteen out of 42 strains were found to have *cag PAI homB* gene and *jhp0562* gene region (38.09%) together.

Key Words: *cagA* 3' polymorphisms, *Helicobacter pylori*, *homB*, *jhp0562*, *jhp0563*



Effect of *rpoB* Gene Mutation on Minimal Inhibitory Concentration of Rifampicin and Rifabutin in *Mycobacterium tuberculosis*

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The aim of the study was to evaluate the effects of different *rpoB* gene mutations found by using DNA sequence analysis on the MIC's of rifampicin (RIF) and rifabutin (RBU) in MDR *M. tuberculosis* isolates using agar proportion method.

Forty clinical isolates of *M. tuberculosis* complex (MTBC) having *rpoB* gene mutations were studied. *M. tuberculosis* H37Rv (ATCC 27294) was used as a quality control strain. Study was performed using agar proportion method and the results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) M24-A document 2003.

RIF and RBU MICs of 40 MDR *M. tuberculosis* isolates with 18 different point mutations on 8 different codons of *rpoB* gene were determined. Although there were a few differences between RIF and RBU MIC values, there was a correlation between them. Almost all isolates high-level resistant to RIF were also resistant to RBU. However, RBU may remain active against some RIF resistant strains with certain mutations.

In conclusion, it was found that *rpoB* gene mutations led resistance to RIF and RBU in MDR *M. tuberculosis* clinical isolates. Moreover, cross-resistance was found between two drugs. Although RBU resistant strains were also resistant to RIF, some of the RIF resistant strains with certain mutations in *rpoB* gene region were found as susceptible to RBU. That's why it is very useful to determine *rpoB* gene mutations and to use RBU as an alternative drug according to the antimicrobial susceptibility testing results for RIF resistant *M. tuberculosis* isolates.

Key Words: *rpoB* gene mutations, antimicrobial susceptibility, rifabutin, rifapentin



Traditional Methods and Sequence Analysis System in the Identification of Non-Tuberculosis Mycobacteria

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INTRODUCTION: In the recent years, due to the increasing incidence of Acquired Immunodeficiency Syndrome and widespread use of chemotherapeutic drugs in cancer therapy, the observed frequency of MOTT infections increased. In parallel to the increase in frequency, rapid identification of these species has gained importance for the determination of accurate and early treatment approach. Conventional and molecular methods are used in the species-level identification of mycobacteria. Conventional methods have numerous difficulties in the species-level identification of MOTT and clinical diagnosis of infections caused by MOTT. Various molecular methods have been developed for rapid and reliable identification. Mycobacterial species can be discriminated by the sequence analysis of some of genetic regions. 16S rRNA and Hsp65 are the most frequently used genetic regions in the species identification.

METHOD: In this study, 90 MOTT strains obtained from the four centers, Samsun, İstanbul, Ankara, Malatya were identified by the sequence analysis of 16S rRNA and Hsp65 genetic regions. Additionally, certain biochemical tests were done in order to support the identification and for the phenotypic characterization of the strains. All of the strains (n= 90) were identified by the sequence analysis of the two genetic regions. The application and evaluation of biochemical tests which were done in comparison to sequence analysis were problematic.

RESULTS and CONCLUSION: The results of our study showed that mycobacteria species have very close genotypic similarities to each other. Hsp65 gene region should be used as an alternative when there is a difficulty in the species identification by 16S rRNA sequence analysis which is accepted as the gold standard. In spite of the advances in molecular methods, phenotypic tests, although time-consuming and cumbersome, are still needed in the discrimination of certain species

Key Words: MOTT, DNA sequence analysis, biochemical tests.

Mycology

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Gastrointestinal Mucormycosis Causing an Acute Obstruction in the Neonate Patient

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INTRODUCTION: Mucormycosis is a rare opportunistic invasive fungal infection caused by *Mucorales* of class Zygomycetes that occurs in immunocompromised human hosts. Mucormycosis of the gastrointestinal tract is rare. Here we present a rare case of a female neonate with gastrointestinal mucormycosis.

CASE REPORT: A female neonate was admitted to our hospital with complaints of abdominal distention and vomiting. Her systemic examination was normal except for diffuse abdominal tenderness. Results of laboratory investigations revealed a white blood cell count of 14.000/mm³, and a C-reactive protein of 101 mg/L (reference: 0 to 5 mg/L). Clinical and radiologic ileus in patients thought to have been operated. 30 cm ileal resection was performed in the areas of necrosis seen in the ileum of the patient. Biopsy from the bowel with numerous broad aseptate hyaline fungal hyphae branching at right angles suggestive of mucormycosis (Figure 1). The peritoneal fluid and the blood cultures were negative for organisms and fungi. Ileostomy closure was done after 3-week administration of IV liposomal amphotericin B that was well tolerated. The child is thriving well and gaining weight after ileostomy closure.

CONCLUSION: The high mortality results from lack of clinical suspicion coupled with inadequate surgery and antifungal therapy. To conclude, GIM should be considered in neonates with a clinical picture of ileus and NEC, who have if not breastfeeding negligible enteral feedings and treatment with multiple antibiotics and prolonged neutropenia. Aggressive early surgery followed by intravenous amphotericin B after histological diagnosis is the mainstay of treatment.

Key Words: Amphotericin B, gastrointestinal mucormycosis, neonate

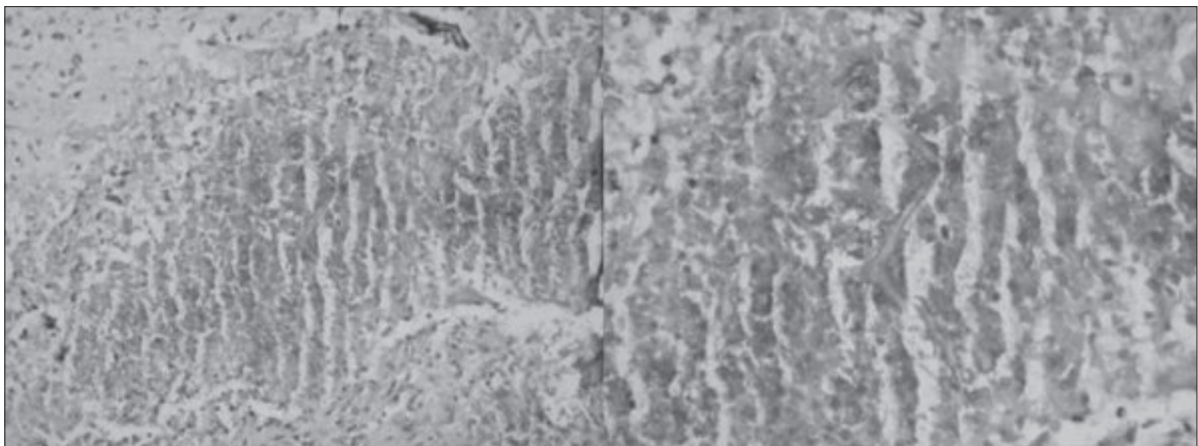


Figure 1. Aseptate hyaline fungal hyphae.



An Outbreak of *Fusarium solani* Endophthalmitis After Cataract Surgery in an Eye Training and Research Hospital in Istanbul

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PURPOSE: To report an outbreak of *Fusarium solani* endophthalmitis after uneventful cataract surgeries performed on the same day in the same operating room.

METHODS: Nine patients underwent phacoemulsification at 4th Clinic of Beyoglu Eye Training and Research Hospital in Istanbul. Cefuroxime axetyl was injected intracamerally from the same vial to all patients at the end of surgery. All patients developed acute postoperative endophthalmitis. Presentation, cultural studies, treatment, clinical responses, risk factors were evaluated.

RESULTS: Cultural and DNA sequence findings revealed *F. solani*. Antifungal therapy was begun and pars plana vitrectomy, intraocular lens and capsule extraction were performed. Corneal involvement was correlated with old age and systemic disease.

CONCLUSION: *F. solani* should be considered in acute postoperative endophthalmitis. This infection can be controlled with early and aggressive combined antifungal and surgical treatment. The patients with corneal involvement had poor prognosis. It is important to use solutions prepared separately for each patient.

Key Words: *Fusarium solani*, endophthalmitis, cataract, antifungal therapy



Trichophyton tonsurans Scalp Carriage Among Wrestlers in a National Competition in Turkey

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Trichophyton tonsurans tinea gladiatorum is an emerging epidemic among combat-sport athletes across the globe. In the present study, we investigated the prevalence of symptomatic and asymptomatic dermatophytic infections among wrestlers in the National Greco-Roman Championship in Turkey. In total, 194 wrestlers from 32 provinces and 72 clubs were examined for scalp, trunk, groin, and toe web dermatophytic infections. We also administered a questionnaire to obtain information on the participants' lifestyles, wrestling characteristics, and risk factors for dermatophytic infections. The hairbrush method was used for scalp and trunk sampling, whereas a cotton swab was used for groin, toe web, and mat sampling. Three wrestling mats in the gymnasium were surveyed for dermatophytes using the touch preparation method. A total of 17 (8.8%) wrestlers harbored dermatophytes, and 22 strains were isolated: 13 (59.1%) *T. tonsurans* and 9 (40.9%) *T. rubrum*. These isolates were found on the scalp (8), trunk (2), forearm (1), hand (1), groin (3), and feet (7). In addition, we recovered 8 dermatophyte strains from the 150 mat samples (5.3%): *T. rubrum* in 6 samples (75%) and *T. tonsurans* in 2 samples (25%). *T. tonsurans* was only recovered from 11 out of 194 (5.7%) wrestlers. Scalp carriage represents the predominant (72.7%) clinical picture of a *T. tonsurans* infection in these Greco-Roman wrestlers in Turkey.

Key Words: Anthropophilic, asymptomatic carrier, dermatophyte, *Trichophyton tonsurans*, wrestling

Slime Production and Adhesion Gene Expression are not Associated with Recurrent Vulvovaginal Candidiasis

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The aim of this study is to investigate the slime production and adhesion gene expression ability of *Candida* strains isolated from vulvovaginal candidiasis. We investigated the slime production of *Candida* strains among 189 isolates of *Candida* isolated from patients with acute or recurrent vulvovaginal candidosis (RVC). Slime production was evaluated by growing organisms in Sabouraud broth with 8% glucose and examining the walls of the tubes for the presence of an adherent slime layer. HWP and ALS-expression, assayed using PCR, was compared using slime activity on macro-tube surfaces. 43.8% of the isolates of acute cases produced slime; 9.4% of the isolates were moderately to strongly positive, 34.4% were weakly positive and 56.2% were not slime producers. 44% of the isolates of RVC produced slime; 16% of the isolates were moderately to strongly positive, 28% were weakly positive, and 56% were not slime producers. We investigated agglutinin like sequence (ALS) and Hyphal Wall Protein (HWP) expression of *Candida* strains among 85 slime positive isolates of *Candida* isolated from patients with 31 acute and 54 RVC. 61.3% of the isolates of acute cases were ALS1 positive, while 55.5% of the isolates of RVC were ALS1 positive. 42% of the isolates of acute cases were HWP1 positive, while 52% of the isolates of RVC were HWP1 positive. The results of this study failed to provide evidence for the existence of slime production in frequent RVC compared to unfrequent RVC. No correlation has been found in RVC and acute vaginitis patients in terms of slime production and adhesion gene functions. RVC rarely have recognizable precipitating or causal factors. No fungal virulence factors have been identified to explain the repeated attacks.

Key Words: Vulvovaginal candidiasis, slime, adhesion gene

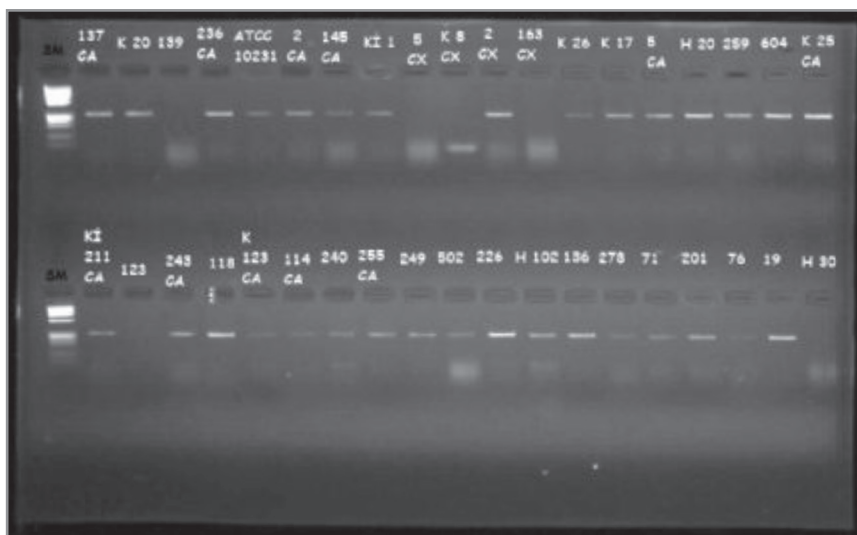


Figure 1. Electrophoresis, PCR results.



A Case of Rhinoorbital Mucormycosis Caused by *Rhizopus oryzae* in a Leukemic Patient with a Literature Review from Turkey

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Mucormycosis (Zygomycosis) is a rare, invasive, opportunistic fungal infection of the paranasal sinuses, caused by a fungus of the order *Mucorales*. We report a case of rhinoorbital mucormycosis caused by *Rhizopus oryzae* in an acute lymphoblastic leukemia and review the 79 cases of Mucormycosis reported in the last ten years from Turkey. In our case the diagnosis was made with endoscopic appearance, computerized tomography (CT) of the paranasal sinuses and culture of the surgical materials. The infecting agent was identified by conventional methods and identity was proven by sequence analyses of ITS region. After aggressive surgical debridement under endoscopic vision and parenteral amphotericin B therapy, the patient recovered completely. In our Turkish literature review, rhinocerebral manifestations were the most common form of the mucormycosis (64 cases), followed by pulmonary form (6 cases). The most common risk factor was hematological malignancies (32 cases) and diabetes mellitus (32 cases), similar to those reported from the worldwide. The etiologic agents isolated were *Rhizopus* spp., *Mucor* spp., *Rhizomucor* spp., *Rhizopus oryzae*, *Mucor circinelloides*, and *Absidia corymbifera*. Although various treatment modalities were used, Amphotericin B was the mainstay of therapy. Mortality rate was 49.4% in the reviewed 79 cases. It seems that strong clinical suspicion and early diagnosis along with aggressive antifungal therapy and endoscopic sinus surgery have great importance for better prognosis in patients with mucormycosis.

Key Words: Mucormycosis, Zygomycosis, rhinoorbital mucormycosis, *Rhizopus oryzae*



Diagnosis of Invasive Aspergillosis by Various Microbiology Methods

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It was aimed to evaluate the diagnostic potential of culture, direct microscopy, the galactomannan, 1,3 beta-D-glucan and real-time PCR assay for IA (invasive aspergillosis).

Various clinical specimens of the 87 patients with suspicious IA infections treated in Erciyes University Gevher Nesibe Hospitals clinics between December 2007 and November 2008 were included in this study. Culture and direct microscope of clinical specimens were performed. *Aspergillus* antigen was investigated in sera specimens by enzyme-linked immunosorbent assay (ELISA) for galactomannan (Platelia *Aspergillus*, BioRad, France) and an assay for BDG (Fungitell; Associates of Cape Cod). DNA was investigated real-time polymerase chain reaction (PCR) (light-cycler Roche diagnostics, Australia) in sera specimens.

It was analyzed 87 patients at high risk for IA including 57 patients with IPA (invasive pulmonary aspergillosis) and 30 control patients and diagnosed 3 proven IA cases, 33 probable IA cases and 21 possible invasive fungal infections.

Fifty-seven patients had proven, probable and possible IA that were positive for BDG assay (68%), for GM assay (38.5%) and for PCR (14%).

The use of a combination of the BDG and the GM assay increased the sensitivity to 71.9%, decreased the specificity to 91%. The use of a combination of the BDG and the GM and PCR assay increased the sensitivity to 73%.

Among these screening tests for IA, BDG test was the most sensitive at predicting the diagnosis of IA in high-risk patients and a combination of the three should improve the diagnosis of IA.

Key Words: *Aspergillus*, 1,3 β -D-glucan, polymerase chain reaction (PCR), galactomannan (GM), culture, direct microscopy, invasive aspergillosis.



Galactomannan Antigenemia in Pediatric Cancer Patients

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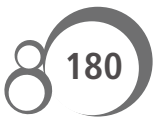
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BACKGROUND: Invasive aspergillosis is the most serious life-threatening opportunistic invasive mycosis and cause of morbidity and mortality due to the inability identify in pediatric cancer patients. Diagnosis is based on a combination of imaging and a number of laboratory techniques. In recent years, serum galactomannan (GM) detection is considered to be a useful test for early diagnosis and follow-up of invasive aspergillosis. Although GM antigenemia has been well studied in the detection of infection in adult patients, little is known in pediatric cancer patients. This study aimed to diagnose and follow-up GM antigenemia in invasive aspergillosis pediatric cancer patients.

METHODS: From January 2008 to December 2010, 383 pediatric cancer patients [(age: 3 months-16 years) (females: 143, males: 240)] hospitalized in our haematology-oncology units for receiving intensive chemotherapy and/or hematopoietic stem cell transplantation were studied retrospectively. We searched the expression of GM antigen by Platelia TM enzymeimmunoassay (EIA) in 796 serum samples. In addition the cultivation of the clinical samples (blood: 33, sputum: 1) and polymerase chain reaction (PCR) of three sera were performed in GM positive patients.

RESULTS: The serum samples having OD index \geq or 0.5 ng/mL with Platelia *Aspergillus* TM EIA test were considered as GM positive according to test procedure. GM were found as positive in one and multiple serum samples from 19 (4.9%) and 14 (3.6%) patients respectively (total: 33). The *Aspergillus* species were not isolated from any blood cultures. *A. fumigatus* grew three times in repeated sputum cultures of 1 patient. (direct microscopy+) OD index: 0.5, 0.6, 1.0 respectively). The results of PCR were negative of three patients (in one serum sample OD index: 0.59, 0.6, 0.76 respectively). The findings of direct examination, culture, GM, PCR, clinical and radiological data were evaluated together.

Key Words: Invasive aspergillosis, pediatric cancer patients, galactomannan



Diffuse Infiltration of *Aspergillus hyphae* was Observed in the Thyroid Gland with Multinodular Guiter

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INTRODUCTION: *Aspergillus* is a fungus that is found in every region of the world and causes a wide range of disorders, including pulmonary and nasal allergy, chronic pulmonary infection, and invasive disease. We aimed to present this case report, because fungal infectious of thyroid gland is uncommon.

CASE SUMMARY: A 35 year-old woman presented with a thyroid mass, weakness and shortness of breath for three years. On physical examination she had a diffusely enlarged thyroid gland and multiple nodules. There was no sign of immunospression. The patient had a history of farming and raising livestock. T3, T4, and TSH were 2.46 pg/mL, 1.14 pg/mL, and 40.7 μ IU/mL, respectively. She was operated. Histological examination of operational specimens showed hyperplasia of the epithelial cells and colloid-rich adenomatoid nodules with haemorrhagic and cystic degeneration. However, having been examined with a microscope, PAS positive hyphae, which are next to the thyroid capsule, dividing into branches of 45 degrees, and conidia were detected. Moreover there were some ischemic changes next to the thyroid capsule on the thyroid tissue. It was detected that *Aspergillus* hyphae caused some changes on the thyroid tissue, follicular and vascular wall related to infarct.

CONCLUSION: In our case, we, coincidentally, found aspergillosis in the thyroid of the patient who was operated for multinodular guiter. Our patient had no diabetes mellitus, alcoholism, past respiratory infection, immunodeficiency status, and a history of trauma. Because the patient is a healthy individual, it is interesting that *Aspergillus hyphae* causes some changes on the thyroid.

Key Words: Aspergillosis, thyroid gland, healthy individual



Nosocomial Infections Associated with *Candida* species in a Turkish Training Hospital: Evaluation of Last Four Years

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In recent years, an increase in the frequency of nosocomial infections due to *Candida* species has been observed, especially among critically ill or immunocompromised patients. The aim of this study was to evaluate the trend in incidence of nosocomial infections associated with *Candida* species together with potential risk factors in an 1100-bed Turkish Tertiary Care Hospital in a 4-year period. A total of 61 infection episodes were identified in 61 patients. Of the 61 patients, 28 were women (46%) and 33 were men (54%). *Candida albicans* was the most common species (33/61, 54%) and non-*albicans* species accounted for (28/61) 46% of all infections. The most common non-*albicans* sp. isolated was *C. glabrata* (8/61, 13.11%) followed by *C. tropicalis* (7/61, 11.4%), *C. parapsilosis* (7/61, 11.4%), *C. stellatoidea* (6/61, 9.8%), respectively. The most frequent risk factors possibly associated with infections due to *Candida* species were urinary catheterisation (98.3%), total parenteral nutrition (88.5%) and presence of central venous catheter (72.1%). Our result show the fact that the incidence of infections caused by *Candida* species is increasing, although the most common isolated candida species were *C. albicans*, further investigation should performed to determine potential reasons of increasing incidence of infections caused by non-*albicans* species.

Key Words: *Candida* species, nosocomial infections



Analysis of Fatty Acid Methyl Ester (FAME) for the Identification of *Candida* species

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Candida species are frequently isolated in cases of fungal infections and reliable identification methods in the routine laboratory is mandatory. The aim of this study was to evaluate the performance of fatty acid methyl ester (FAME) analysis in identification of *Candida* species.

Vaginal samples were evaluated for the presence of yeasts, besides other agents of vaginitis. All of the isolates were identified initially by conventional methods. Cellular fatty acids of the yeasts were extracted and separated into their fatty acid methyl esters (FAMEs) by MIDI Microbial Identification System utilising an Agilent Technologies 6890N gas liquid chromatograph with a G2614A auto sampler and a 6783 injector. After flame ionisation, FAME peaks were analysed by MIDI Microbial Identification System, software version YEAST28.

Out of 30 yeast isolates, 18 (60%) *C. albicans*, 10 (33.4%) *C. glabrata*, 1 (3.3%) *C. tropicalis* and 1 (3.3%) *C. krusei* were identified by using both methods. However, we observed *C. glabrata* can easily be misidentified as *S. cerevisiae* with FAME analysis. Similarly there was a risk for misidentification for *C. albicans* strains with *C. tropicalis* and *C. lusitanae*.

The results of the present study demonstrated that FAME analysis can be used as an alternative method in yeast identification preferably in combination with other methods. More studies with large series of yeasts are needed to verify the results of this study.

Key Words: *Candida*, FAME, identification

Relationship Between *ALS1* and *HWP1* Genes and Slime Production in Clinical Isolates of *Candida albicans*

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AIM: Our aim is to explore presence of *ALS1* and *HWP1* genes by multiplex polymerase chain reaction (PCR) in *C. albicans* strains isolated from various clinic samples and to evaluate slime factor by microplate and modified tube adherence test methods in order to control phenotypic reflection of these genes.

MATERIALS and METHODS: By multiplex polymerase chain reaction (PCR) method, presence of agglutinin-like sequence 1 (*ALS1*) and hyphal wall protein1 (*HWP1*) genes were investigated in 206 *C. albicans* strains which were isolated from various clinical samples between June 2010 and September 2010. In addition, phenotypic identification of slime formation by microplate and modified tube adherence tests were performed.

RESULTS: Presence of *ALS1* gene was detected in 53.9%, while *HWP1* gene was present in 5.3% of all strains. It was seen that *ALS1* gene was also present in all strains in which *HWP1* gene existed. Of the phenotypic tests, positive slime formation was detected in 34.5% of strains by microplate method, while 16.5% by modified tube adherence test. There was significant relationship between presence of genes and microplate method, while there was no significant relationship with modified tube adherence test. Slime production status of strains and presence of genes according to isolated source is shown in Table 1.

CONCLUSION: It was found that there was *ALS1* gene presence in approximately half of clinical isolates of *C. albicans*. A significant relationship was found between presence of these genes and slime production detected by microplate method but not modified tube adherence test.

Key Words: *ALS1*, *C. albicans*, *HWP1*, microplate method, modified tube adherence test, slime factor

Table 1. Slime production status of strains and presence of genes according to isolated source

Strains isolated from the specimens	Presence of <i>ALS1</i> gene		Presence of <i>HWP1</i> gene		Positive slime production by Microplate test		Positive slime production by tube adherence test	
	n	%	n	%	n	%	n	%
Urine (n= 82)	43	52.4	4	48.8	26	31.7	15	18.3
Vajinal swab (n= 77)	37	48	3	3.9	26	33.8	8	10.4
Wound (n= 17)	7	41.7	2	11.8	6	35.3	5	29.4
Blood (n= 13)	11	84.6	1	7.7	7	53.8	2	15.4
Respiratory specimens (n= 12)	8	66.7	1	8.3	5	41.7	2	16.7
Peritoneal fluid (n= 3)	3	100	-	-	-	-	2	66.7
Cerebrospinal fluid (n= 2)	2	100	-	-	1	50	-	-
Total (n= 206)	111	53.9	11	5.3	71	34.5	34	16.5



Identification of Superficial Fungal Infections at the Elderly Living in Nursing Home

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In this study, we aimed to determine the frequency and distribution of pathogens causing fungal diseases among residents of the Kahramanmaraş Nursing Home. Eighty-eight residents in the Kahramanmaraş Nursing Home were included in the study and examined for fungal diseases. Dermatologic examinations of the elderly with health-related complaints and suspected fungal lesions generally revealed findings of erythema, rash, eczema-like skin changes, and pruritus in the hands and feet. Scraping samples acquired from the keratinized tissues with suspected fungal lesions such as hair, skin, and nail, were placed into petri dishes and analyzed with microbiological methods including direct microscopic examination and culture method. Fungal growth in the cultures were identified at species and genus level based on the colony morphology, presence of pigments, and other characteristics. Among our study population comprised of 88 people aged between 60-105 years, 41 (46.59%) suspected fungal lesions were determined in 37 (42.04%) people. While 9 (24.31%) of those 37 patients were female, 28 (75.67%) were male. Among 41 dermatophytosis cases; prediagnosis was tinea pedis for 25 (60.97%), tinea unguium for 13 (31.7%), tinea unguium + tinea manuum for 1 (2.43%), tinea manuum for 1 (2.43%), and tinea corporis for 1 (2.43%). Direct microscopic examination revealed fungal hyphae and spores. Culture analysis displayed fungal growth in 15 (36.58%) samples. In those samples, we identified *Candida* spp. in 10 (66.66%), *Trichophyton rubrum* in 2 (13.33%), *T. mentagrophytes* in 2 (13.33%), and *T. mentagrophytes* + *Candida* spp. in 1 (6.66%).

Key Words: Fungal infections, dermatophytosis, nursing home



In Vitro Haemolytic Activities of *Candida albicans* Isolated from Oral Cavities of HIV Positive Patients

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OBJECTIVES: The aim of this study was to evaluate in vitro haemolytic activities as a virulence factor of oral *Candida albicans* isolates from HIV infected patients and healthy controls.

METHODS: In this study 52 *C. albicans* strains isolated from HIV positive subjects' and 22 *C. albicans* strains isolated from healthy controls' oral rinse samples were investigated. Identification was based on API 20C AUX system (Biome-rioux, Marcy l'Etoile, France) and polymerase chain reaction (PCR) with species-specific primers. In all experiments, *C. albicans* NIH A, NIH B and Ca26555 were used as reference strains. Haemolytic activity (Hz) was determined by using the blood agar plate assay methods. Plates were incubated at 37°C in 5% CO₂ for 48 hours. The presence of a distinct translucent halo around the inoculum's site, viewed with transmitted light, indicated positive haemolytic activity. Haemolytic activity was expressed as the ratio of the colony diameter to the diameter of the translucent zone of haemolysis. *C. albicans* ATCC 90028 and *C. parapsilosis* ATCC 2201 were employed as positive and negative controls, respectively.

RESULTS: The Hz values ranged from 0-3.57 for the HIV positive group and from 0-2.88 for the controls. Higher haemolysin activities were detected in the test group isolates than in the control isolates ($p < 0.05$). The Mann-Whitney U test (The Mann-Whitney-Wilcoxon) used for assess difference between control and patient groups.

CONCLUSION: This result suggests that the degree of extracellular haemolysin activity may be important for successful oral colonization of *C. albicans* in HIV positive subjects.

Key Words: *Candida albicans*, HIV, virulence factor, haemolytic activity



The Species Distribution of Yeasts and Moulds Isolated in a Tertiary-Care Military Hospital in Turkey Between 2001-2010

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Despite significant advances in the diagnosis, prevention, and treatment of fungal infection in critically ill patients, it remains a major cause of morbidity and mortality. During the past decade significant changes have occurred in the incidence and the epidemiology of these infections. The purpose of this study was to evaluate the species distributions of yeast and mould strains isolated from various specimens at the department of medical microbiology in years between 2001 and 2010. In this ten year period, 11.319 clinical specimens were sent to the mycology laboratory. Fungal growth occurred in 2980 (26.3%) of clinical specimens obtained from 2431 patients. A total of 2868 yeasts and 151 mould strains were identified. Of the yeast isolates, 2776 (96.8%) were *Candida* spp., 41(1.4%) *Malassezia* spp. and 31 *Trichosporon* spp. (1.1%). The mostly isolated *Candida* species were *C. albicans* (n= 1365, 47.6%), followed by 226 *C. glabrata* (7.9%), 224 *C. parapsilosis* (7.8%), 201 *C. tropicalis* (7.0%). Interestingly, the number of *C. parapsilosis* species (n= 116, 34.3%) isolated in blood cultures was the second most after *C. albicans* (43.5%). Of the mould isolates, *Aspergillus* spp. (n= 92; 60.9%) were the mostly isolated mould species. The thirty-two of them were *Aspergillus fumigatus* (21.2%), 27 *A. flavus* (17.9%) and 20 *A. niger* (13.2%). Additionally, 15 *Trichophyton rubrum* (9.9%) and 13 *T. mentagrophytes* (8.6%) isolates were recovered during this period. In conclusion, *Candida* spp. and *Aspergillus* spp. were the most common fungal species regardless sample type, years, and the department where the patient was hospitalized, as in the literature.

Key Words: *Candida* species, yeasts, mould, yeast identification, mould identification



Investigation of Fungal Infections in a Teaching Hospital

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BACKGROUND: The aim of this study is to determine the fungal infections and their causative agents distributions, the resistance of the fungi obtained as well as the response of patients to antifungal treatment and to introduce to the clinical use the quick, simple and cheap antifungal sensitivity and identification method which is of high specificity and sensitivity.

METHOD: Data collected from the medical records of patients with fungal strains included demographic characteristics, underlying diseases, invasive procedures, and outcome. The strains were identified through germ tube test, clamdiopspor formation and a commercial kit labeled API 20C AUX.

RESULTS: Totally 125 fungal strains isolated from the patients (61 female and 49 male) were evaluated. The fungus obtained in our study 37.3% of the patients included in our study were hospitalized in Surgery care unit, 18.2% of them in Internal unit, and 44.5% of them in other units. Of patients' clinics, 24.5% was found to be consistent with candidemia and 75.5% with candiduria.

The distribution of the strains isolated from both clinical samples is as follows: while 59.2%(74/125) of the strains was *C. albicans*, 15.2% (19/25) *C. tropicalis*, 12.8% (16/125) *C. parapsilosis*, 4.8% (6/125) *C. krusei*, 4% (5/125) *T. asahii*, 1.6% (2/125) *C. kefyr*, 2.4% (3/125) was *C. glabrata*, *C. lipolytica* and *C. lusitanae*, each with one isolate.

CONCLUSION: Our results also show the importance of the definition of the fungal agents isolated at a level of species and of antifungal sensitivity tests. The results also emphasize that clinical findings along with the fungal culture results and the characteristics of the underlying disease are of great importance in the decision to treat fungal infections.

Key Words: Fungal infections, *Candida*, antifungal sensitivity

Investigation of Galactomannan Antigen in Invasive Aspergillosis Suspected Patients

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INTRODUCTION: *Aspergillus* spp. have been widely isolated from the environment. They have caused bronchopulmonary infections via inhalation of their spores. *Aspergillus* spp. have been isolated frequently from clinical specimens due to the increase of immunodeficient patients. The studies showed that invasive aspergillosis is the most second common fungal infection in hospitalised patients in USA. Detection of the invasive aspergillosis in the early stage of the infection is important for the treatment. The gold standard for the diagnosis of invasive aspergillosis is the direct examination and the cultivation of biopsy of lung tissue. But these methods are invasive and sometimes it is impossible because of the patient's conditions. Because of this there is a need for some method that is not invasive and is sensitive to the early stage of the infection. Detection of antigens (beta-glucan or galactomannan), measurements of antibodies and nucleic acid detection techniques are some of them. From these tests the detection of galactomannan is currently used in practice. It is the cell wall component of the *Aspergillus* spp. It is important because the level of galactomannan is proportional to the fungal load in tissue and the level of galactomannan has prognostic value. There are some commercial tests like ELISA and latex agglutination. ELISA test is used frequently to detect galactomannan from serum or bronchoalveolar lavage. It is recommended that serum from the patients suspected of invasive aspergillosis should be sent to the laboratory once or twice per week. In this study we aimed to investigate the presence and level of the galactomannan antigen in the serum of patients by ELISA that was sent to our laboratory.

MATERIALS and METHODS: The sera of 503 immunodeficient patients (230 female, 273 male) that were sent to our laboratory in one year period for the detection of galactomannan antigen level were studied by Platelia *Aspergillus* EIA.

RESULTS and CONCLUSION: The results were evaluated according to the test manufacturer's recommendations and the galactomannan index value accepted as 0.5. The test results of 179 patients (F/M: 87/92) were above the index value of 0.5. While there was a single serum sample sent to our laboratory from 109 patients, from 70 patients multiple serum samples were sent to the laboratory. Galactomannan is one of the tests that gives physicians an early diagnosis opportunity. Multiple galactomannan index values are necessary in the diagnosis and monitoring of patients. Galactomannan EIA is a simple and non-invasive test that does not give the patient any discomfort and gives rapid results in the evaluation of the patient's clinic.

Key Words: *Aspergillus* spp., galactomannan antigen



A Retrospective Evaluation of In Vitro Direct Immunofluorescence (IF) Test for *Cryptosporidium* Oocysts in 3-Year Period

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INTRODUCTION: Cryptosporidiosis is a zoonotic infection. It can cause waterborne and foodborne outbreaks. *Cryptosporidium* species are important causes of diarrhea, especially in children and immunocompromised patients. Diagnosis of cryptosporidiosis is generally based on testing stools for the presence of oocysts by staining or for the presence of oocyst wall antigens by immunoassays. In this study, we aimed to evaluate retrospectively the results of in vitro direct immunofluorescence (IF) test which is used in our laboratory for the detection of *Cryptosporidium* oocysts.

MATERIALS and METHODS: This study includes the stool samples sent to Parasitology Laboratory, Ondokuz Mayıs University Medical Faculty Hospital between January 2008-November 2010 for investigation of the presence of *Cryptosporidium*. IF test was used to detect the presence of *Cryptosporidium* oocysts in stool and it was performed according to the recommendations of the manufacturer (Cellabs, Crypto/Giardia Cel Australia). Patient records (total number of patients, the number of positive patients, the general characteristics and clinical data of patients) were obtained from computer-aided automation system that is used at our hospital.

RESULTS: In this 3-year period, a total of 390 stool samples were sent to the laboratory for the detection of *Cryptosporidium* oocysts by IF test. 183 samples (46%) were positive [88 males (48%), 95 females (52%)]. Gastroenterology department (88 samples, 48%) for adults was in the first place and followed by pediatric haematology (13 samples, 7%). Only 32 patients (18%) had an immunocompromised condition (cancer, AIDS, immunosuppressive drugs, organ transplants, etc.).

CONCLUSION: The severity of cryptosporidiosis varies depending on parasite and host characteristics. It may be a big problem in developed and developing countries. Therefore, it is important to detect the organism properly from stool specimens for the management of the disease, especially in immunocompromised patients.

Key Words: Immunofluorescence, cryptosporidium, stool, IF



Distribution of *Candida* Species Isolated from Various Clinical Specimens

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INTRODUCTION: *Candida* spp. represent organism that are frequent in the nature, and can cause opportunistic infections associated with high mortality and morbidity rates under predispose factors such as the use of broad spectrum antibiotics, immune suppression, application of invasive catheter, major surgical procedures. In risk groups, extensive use of common prophylactic drugs may cause selection of resistant species or acquired resistance among susceptible organisms. True identification of organism at species level is thus important for empirical treatment modalities. The objective of this study was to analyze retrospectively the species distribution of clinical *Candida* isolates according to the body site source from which the specimens were obtained, hospital departments of the patients, over a 3-year period in Ondokuz Mayıs University, Medical Faculty, Microbiology Department.

MATERIALS and METHODS: Clinical specimens obtained from various departments in Samsun, Ondokuz Mayıs University, Medical Faculty, Microbiology Laboratory were investigated during a 4-year period from January 2007 to January 2011. All specimens were inoculated onto blood agar, eosin metilen blue (EMB) agar, sabouraud dextrose agar and incubated for up to 7 days at both 30°C and 37°C prior to being discarded as negative for fungal growth. For the identification of the isolates, we employed conventional procedures such as germ tube production, microscopic morphology on corn meal Tween 80 agar, as well as commercial methods such as CHROMagar *Candida* API 20C AUX. Repeat samples from patients were excluded. Hospital wards were grouped into four main departments, i.e., intensive care units (ICU), surgical services, internal medicine departments and pediatric services.

RESULTS: 1895 *Candida* isolates were included in this study. The distribution of *Candida* strains were as follows; 3943 from urine, 285 from sputum, 327 from blood, 92 from vaginal swabs, 78 from tracheal aspirate, 72 from sterile body fluid, 61 from exuda, 25 from catheter, 8 from gaita. Most of the clinical specimens obtain from internal medicine departments. The species of *Candida* strains was as follows; 1021 *C. albicans* (53.8%), 310 *C. tropicalis* (16.3%), 180 *C. parapsilosis* (9.4%), 92 *C. glabrata* (%4.8), 76 *C. krusei* (4.0%), 13 *C. lusitaniae* (0.6%), 9 *C. guilliermondii* (0.4%) ve 9 *C. dubliniensis* (0.4%).

CONCLUSION: Our study demonstrated that the proportion of non-albicans *Candida* species is increasing substantially. Because of the antifungal resistance of these species, causative pathogens were isolated according to their species and antifungal susceptibility tests were performed.

Key Words: *C. albicans*, non-albicans *Candida*, identification



Nosocomial Bloodstream Yeast Infections in a University Hospital in Turkey: A 3-Year Survey

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INTRODUCTION: The incidence of nosocomial fungal infections has increased substantially over the last two decades. *Candida* spp. have become the fourth most common cause of nosocomial bloodstream infections. Candidemia is associated with one of the highest rates of mortality of bloodstream infections. The aim of the present study was to gather data on the distribution of bloodstream isolates of *Candida* spp. in our hospital.

MATERIALS and METHODS: This study includes the patients hospitalised and diagnosed as fungemia at Ondokuz Mayıs University Hospital between January 1, 2008 and December 30, 2010 whose blood cultures sent to our microbiology laboratory. After fungal growth was observed in blood cultures, the yeast cells were inoculated onto Sabouraud dextrose agar. They were incubated aerobically for 48 h, at 35°C, and yeast colonies grew. The colonies were identified by conventional yeast identification methods, such as germ-tube formation test, chlamyospore formation and morphology on cornmeal agar-Tween 80 and ID 32C yeast identification system according to the manufacturer's instructions. Susceptibility of isolates to amphotericin B and fluconazole were determined by E-test.

RESULTS: Of all 294 yeast isolates, *C. albicans* was the dominant species (40.8%), followed by *Candida parapsilosis* (26.1%) and *C. tropicalis* (6.1%). Two *C. krusei* isolates were resistant and eight *C. krusei* isolates were dose-dependent susceptible to fluconazole. Also, two *C. glabrata* isolates were dose-dependent susceptible to fluconazole. Two *C. krusei* isolates showed high MIC's of amphotericin B (1 and 1.5 µg/mL).

CONCLUSION: Our survey indicated *C. albicans* continues to be the species most commonly isolated from *Candida* bloodstream infections in our hospital while antifungal resistance was uncommon.

Key Words: Bloodstream infections, candidemia, *Candida*



Distribution of *Aspergillus* Species Isolated from Hospitalized Patients in a University Hospital in Turkey

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INTRODUCTION: *Aspergillus* species are common on the major land, air, plants and decaying material throughout the world. Especially immunosuppressed patients are under the risk of invasive aspergillosis, and in consequence of extensive use of immunosuppressor medications and broad spectrum use of antibiotics, *Aspergillus* species gain importance among infectious diseases. Infections are presented with various clinical manifestations. In this retrospective study was aimed to investigate the distribution of *Aspergillus* species isolated from hospitalized patients.

MATERIALS and METHODS: *Aspergillus* spp. isolated from samples of the patients with suspected fungal infections between April of 2007 and April of 2011, were investigated. The samples were incubated in 25°C and 35°C on brain-heart-infusion agar supplemented with blood and on sabouraud dextrose agar. Gram and Giemsa stained samples were also examined by microscopy. Mold type of fungi were identified by conventional techniques.

RESULTS: A total of 43 *Aspergillus* species were isolated from clinical samples in this study period. Samples were from chest diseases, internal medicine and emergency in order of frequency. Distribution of the, *Aspergillus* species was as the following; 33 (76.7%) *Aspergillus fumigatus*, 8 (18.6%) *Aspergillus flavus*, 2 (4.6%) *Aspergillus niger*. *Aspergillus* species were isolated most frequently from sputum and tracheal aspirate samples.

CONCLUSION: In the last three decades, in accordance with the increase in the number of immunocompromised patients and their prolonged life-span, the incidence of aspergillus infections has increased. *Aspergillus* spores are found everywhere, so it is impossible to totally prevent it. As conclusion, we suggestions are prevention of disease for those who are immunosuppressed. This means minimizing dusty environment exposure, using HEPA filtration or using N95 masks for, high risk patients in the hospital. If exposure is unavoidable, prophylactic antifungal medication is available too.

Key Words: Aspergillosis, *Aspergillus* species, hospitalized patients



The Rapid Identification of the *Candida* Species in Blood Stream Infections

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INTRODUCTION: *Candida* bloodstream infections (BSI) contributes to increased length of hospital stay, increased hospital costs and most importantly, increased morbidity and mortality. Although most *Candida* BSI are due to *Candida albicans* about 45% are caused by *Candida tropicalis*, *Candida parapsilosis*, *Candida krusei* and *C. glabrata*. Even with the use of cutting-edge laboratory testing methods, it can take several days for blood cultures to turn positive for yeast and even longer to identify the species. In recent years, several chromogenic media have been developed for the rapid identification of *Candida* species. We aimed to evaluate the usefulness of CHROMagar™ *Candida* for the primary isolation and identification of *Candida* species directly from blood cultures.

MATERIALS and METHODS: Blood culture samples sent to our laboratory from various clinics between December 2010 and April 2011 were incubated in the BacT/ALERT 3D (bioMérieux-SA, France) automated blood culture system. When growth was detected, smear was prepared for gram stain. When yeast cells were detected in the gram stain, 0.1 mL of the blood culture sample was inoculated both of onto CHROMagar™ *Candida* medium (BBL CHROMagar™, USA) and 5% sheep blood agar. CHROMagar plates were incubated at $35 \pm 2^\circ\text{C}$ for 24 hours and 5% sheep blood agar plates were incubated at $35 \pm 2^\circ\text{C}$ for 24-48 hours. After incubation, CHROMagar plates were evaluated in terms of colony morphology and color. After incubation of 5% sheep blood agar plates, the routine identification of each *Candida* species was based on a conventional scheme, which included determination of germ tube production, microscopic morphology on cornmeal agar and sugar assimilation. The identification was supported using the API 32 C AUX System (BioMérieux, Marcy l'Etoile, France).

RESULTS: A total of 44 *Candida* species were isolated from blood samples in this study period. Samples were from oncology, intensive care unit, internal medicine, chest diseases and neurosurgery in order of frequency. Distribution of the microorganisms was as the following; *C. albicans* 19 (43.1%), *C. parapsilosis* 8 (18.1%), *C. tropicalis* 6 (13.6%), *C. lusitanae* 3 (6.8%), *C. glabrata* 3 (6.8%), *C. kefyr* 2 (4.5%), *C. dubliniensis* 1 (2.2%), *C. guilliermondii* 1 (2.2%) and *C. krusei* 1(2.2%). A total of 26 (59%) isolates were *C. albicans*, *C. tropicalis* and *C. krusei*. Identification of *C. albicans*, *C. tropicalis* and *C. krusei* took an average of 24 hours by direct CHROMagar™ *Candida*, whereas it took an average of 72 hours with the routine identification scheme.

CONCLUSION: Identification of the candida species by conventional methods in blood stream infections takes approximately 72 hours and delays the start of the appropriate treatment. However, we showed that identification of *C. albicans*, *C. tropicalis* and *C. krusei* by direct inoculation to the CHROMagar™ *Candida* can be given within approximately 24 hours. Given the significant differences in the susceptibility to azoles among these three *Candida* species, direct isolation and identification could enable clinicians to select quickly the most appropriate antifungal agent. This therefore has the potential to decrease patient morbidity and mortality.

Key Words: *Candida*, blood stream, identification, Chromagar™ *Candida*



The In Vitro Activity of Amphotericin B and Fluconazole Against Clinical *Trichosporon* Isolates

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INTRODUCTION: *Trichosporon* species may be found in soil, water and other environmental sources. This fungus occasionally as a member of the normal microbiota of the skin, human respiratory and gastrointestinal tracts. *Trichosporon* species have been associated with superficial infections. However, in immunosuppressed patients such as solid organ transplantation, malignancy or AIDS *Trichosporon* species can cause disseminated infections. There are very limited data on in vitro activity of antifungal drugs against *Trichosporon* species. The present study was undertaken to determine the antifungal susceptibility profile of *Trichosporon* species by using the E test method.

MATERIALS and METHODS: This study includes the patients samples at Ondokuz Mayıs University Hospital between January 2010-March 2011 whose urine cultures sent to our microbiology laboratory. The urine samples were inoculated onto Sabouraud glucose agar. The colonies were identified by conventional yeast identification methods and ID 32C yeast identification system according to the manufacturer's instructions. The MICs of all isolates antifungal agents (amphotericin B and fluconazole) were determined using E test strips.

RESULTS and CONCLUSION: In our laboratory in a 15 month period, there were 55 *Trichosporon* spp. isolated from urine samples. MIC₅₀ and MIC₉₀ values of 55 *Trichosporon* spp. for amphotericin B were 0.19 µg/mL, 0.75 µg/mL and for fluconazole were 1.5 µg/mL, 6 µg/mL.

Trichosporon species are causative agents of superficial and systemic fungal infections in humans and have an emerging role in immunocompromised patients. The number of *Trichosporon* spp. are increasing in our hospital in last years. We reinforce the necessity of continuous epidemiologic surveillance to follow the dynamics.

Key Words: Amphotericin B, fluconazole, in vitro activity, trichosporon

The Resistance Rates of *Mycobacterium tuberculosis* Strains Isolated from Several Clinical Samples to Antituberculosis Drugs

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INTRODUCTION: Tuberculosis disease is still one of the most important health problems all over the world. Drug resistance comes at the beginning of the difficulties encountered in the control of tuberculosis. Therefore, it is important to follow-up resistance rates to provide prevention and control measures. In this study, we aimed to determine the resistance rates of *Mycobacterium tuberculosis* strains isolated in our laboratory to major antituberculosis drugs.

MATERIALS and METHODS: This study included 161 *M. tuberculosis* isolates that had been isolated from different clinical specimens between July 2007 and December 2011 in Microbiology Laboratory, Medical School, Ondokuz Mayıs University, Samsun. Recurrent samples were excluded. Distribution of the samples that *M. tuberculosis* had been isolated was as the following; sputum 67, aspiration 27, exudate 10, thoracentesis 10, gastric fluid 8, urine 7, tracheal aspirate 6 and other samples 33. After decontamination process, smear was prepared for staining and sample was inoculated to Lowenstein-Jensen medium and MGIT tubes. Antibiotic susceptibility testing of the isolates was performed by BD MGIT 960 (Becton Dickinson, USA) according to the recommendations of the manufacturer.

RESULTS: The resistance rates of the strains to antituberculosis drugs are shown in Table 1.

DISCUSSION: Today, there are significant problems in the treatment of tuberculosis due to the spread of resistant isolates. Multidrug resistance is a condition enabling *M. tuberculosis* complex to resist two or more primary antituberculosis drugs. Multidrug resistance is one of the most important factors that make difficult to control the treatment of tuberculosis. Isoniazid, rifampicin, ethambutol and streptomycin are the primary drugs in the treatment of tuberculosis. In our study, 40 (24.8%) isolates were found to be resistant. Of these isolates, 8 were multi-drug resistant *M. tuberculosis*. Resistance was most common in isoniazid. Although resistance to ethambutol and rifampicin was not observed alone, resistance to these drugs combined with the other antituberculosis drugs was observed. Consequently, resistance in tuberculosis remains a serious problem and we suggest surveillance studies should be done regularly.

Key Words: Antituberculosis drugs, *Mycobacterium tuberculosis*

Table 1. The resistance pattern of *M. tuberculosis* isolates to antituberculosis drugs

Antituberculosis drug	Resistant strain (%)
Isoniazid	21 (13%)
Streptomycin	11 (6.8%)
Rifampicin	-
Ethambutol	-
Isoniazid + Streptomycin	3 (1.8%)
Isoniazid + Rifampicin	1 (0.6%)
Isoniazid + Ethambutol	1 (0.6%)
Isoniazid + Streptomycin + Rifampicin	1 (0.6%)
Isoniazid + Streptomycin + Ethambutol	1 (0.6%)
Isoniazid + Streptomycin + Rifampicin + Ethambutol	1 (0.6%)
Total resistant strains	40

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Investigation of Frequently Seen Intestinal Parasites by ELISA in Patients who Presented to the Emergency Department with Diarrhea: A Point Prevalence Study

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The aim of this study was to determine the point prevalence of intestinal parasites; *Cryptosporidium* spp., *Entamoeba histolytica* and *Giardia lamblia*, among our patients who were admitted to the emergency room (ER), during one day, with acute diarrheal symptoms. The stool samples which had any positive finding like erythrocyte, leukocyte or cyst/trophozoite on direct microscopy were evaluated for further study. *E. histolytica* adhesion, *Cryptosporidium* oocyst antigen, *G. lamblia* cyst antigens were detected from those stool samples by ELISA. Totally 198 patients were presented with diarrheal symptoms to the ER in one day. Macroscopic evaluation revealed 57 (29%) bloody and mucoid; 130 (66%) unformed-liquid appearance and only 1 (1%) normal appearance. 96 had a positive finding on microscopy like leukocyte or erythrocyte; giardia trophozoites were seen just in 3 (2%). Of these 96 stool samples, two had a positive culture for *Shigella* spp., remaining 94 were evaluated for ELISA. *Giardia* antigen was positive in 13 (14%), *Entamoeba* adhesin was positive in 2 (2%) and *Cryptosporidium* antigen was found in none. Macroscopic and microscopic evaluation of stool samples could be misleading for diagnosis. Recently RT-PCR and multiplex-PCR are used for epidemiologic studies. But they are very expensive for routine clinical practice. ELISA seems to be a useful, sensitive and cheaper tool, for the diagnosis of intestinal parasites. Coming to our results, *Giardia* seems to be the main intestinal parasite among our patients.

Key Words: *Cryptosporidium*, amebiasis, giardiasis, point prevalence



Cutaneous Leishmaniasis Cases in Afyonkarahisar

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Leishmaniasis are widespread in Turkey as in the other countries of the Mediterranean region. Cutaneous Leishmaniasis (CL) is an endemic disease, seen mostly in the Southeastern and Mediterranean regions of Turkey. Afyonkarahisar, where CL could be found sporadically, is at Central Anatolia Regions.

In this descriptive epidemiological study, it was aimed to report patients with cutaneous leishmaniasis in Afyonkarahisar. Demographic features of the patients were obtained from Provincial Health Directorate. Only 17 patients were reported between January 2007 and December 2009. Diagnosis of CL has been done by microscopic examination, when *Leishmania* amastigotes were detected.

Three (17.65%) patients were men, where 14 (82.35%) patients women. Age range was between 5-83 years (39.05 ± 25.09). Patients were mostly between 21-40 years of age (35.29%). The prominent demographic features of the patients were as reported from mostly Dinar and Suhut districts, reported at the summer and being farmer. Major touristic sites of Afyonkarahisar are free of this infection, and it has not been reported yet, in any tourist.

Key Words: Cutaneous leishmaniasis, Afyonkarahisar, Turkey



Leech Infestation That Mixed with Upper Respiratory System Infection

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The urban life and industrialization leads to decrease the incidence of many parasitic diseases. Especially, using the supervised water supplies in urban areas decreases of chance of such infestations and limits in rural areas. However, the people who lives in urban areas and have diseases such as kidney stones think that mountain waters may be beneficial for their illness. These kinds of water supplies are generally unsafe, uncontrolled and septic. That is why usage of them can cause some elusive parasitic infestations in people who live in urban areas. It is meaningful to submit the case described in this case report to redolent of the possibility of parasitic infestations in patient who has upper respiratory tract infection symptoms admitted to the physician.

Key Words: Leech, upper respiratory tract infection, *Limnatis nilotica*

Fascioliasis: Report of 3 Cases with Clinical Presentations at Three Different Phases

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Fascioliasis, which is a zoonotic infestation caused by the trematode *Fasciola hepatica* (liver fluke), is primarily a disease of herbivorous animals such as sheep and cattle. Humans become accidental hosts through ingesting uncooked aquatic plants such as watercress. It presents a wide spectrum of clinical pictures ranging from fever, eosinophilia and vague gastrointestinal symptoms in the acute phase to cholangitis, cholecystitis, biliary obstruction, extrahepatic infestation or asymptomatic eosinophilia in the chronic phase. However, it may often be overlooked especially in the acute phase because of vague symptoms. As a result of newly-introduced serological assays facilitating the diagnosis, there has been an increase in the number of reported cases. Here, we report the clinical, laboratory and therapeutic assessment of a series of three cases diagnosed (in order of) one week, three months and one and a half year after presentation of the first symptoms of the disease.

Key Words: *Fasciola hepatica*, hepatitis, triclabendazole

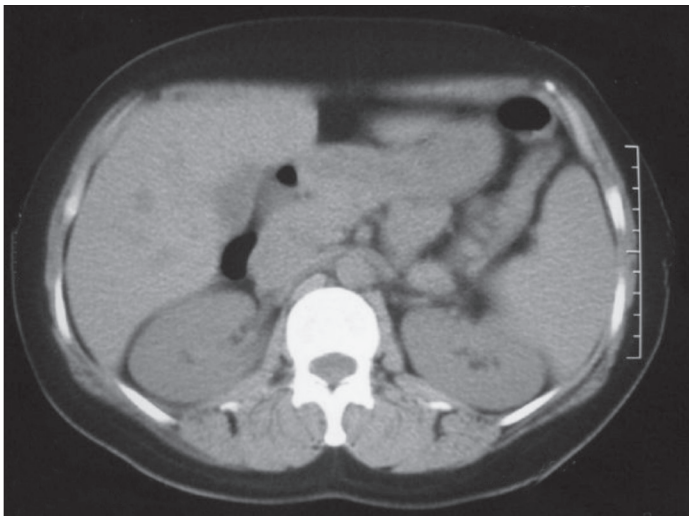


Figure 1. Image of abdominal computerised tomography of the second case showing diffuse periportal enhancement, hypodense areas with ill-defined borders consisting of centrally-located millimetric hyperdense foci.

Evaluation of Oxidative Status in Patients with *Fasciola hepatica* Infection

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AIM: The aim of this study was to evaluate oxidative status by using a novel automated method in patients with *Fasciola hepatica*.

METHODS: Twenty two patients with a diagnosis of *F. hepatica* and 26 healthy volunteers were enrolled in the study. Total antioxidant capacity status (TAC), total oxidant status (TOS) and catalase were measured in them and an oxidative stress index (OSI) was calculated. These measurements were also taken for the control group and the values were compared.

RESULTS: Plasma levels of total TOS and OSI, were significantly increased in patients as compared with healthy controls ($p < 0.001$, $p < 0.001$, $p = 0.001$, $p = 0.008$) respectively. In contrast, TAC level was significantly lower in patients as compared with controls ($p < 0.05$). There was no significant difference between the catalase results of the two groups ($p > 0.05$).

CONCLUSION: Total oxidative status and OSI were increased and total antioxidative status capacity were decreased in patients with *F. hepatica* infection. It is possible to conclude that a high oxidative stress occurs in during *F. hepatica* infection, which may cause severe damage in the liver and body.

Key Words: *Fasciola hepatica*, total antioxidant capacity (TAC), total oxidative status (TOS), oxidative stress index (OSI), novel method

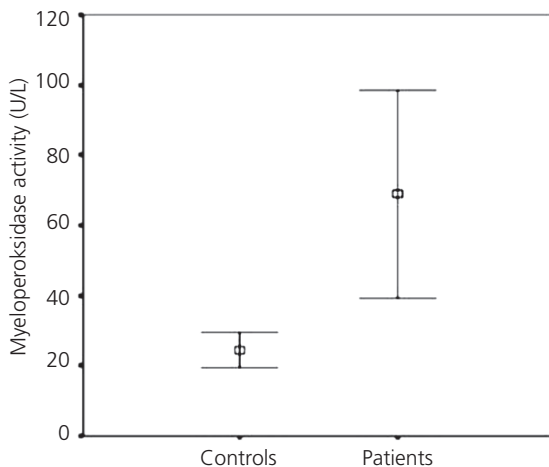


Figure 1. The OSI level of patients and control groups.

Table 1. Serum oxidative status of patients and healthy controls

Parameters	Patients (n= 22) Median ± IQR	Control (n= 26) Median ± IQR	p
TAC	1.14 ± 0.13	1.29 ± 0.15	0.029
TOS	136.40 ± 37.80	10.40 ± 2.43	< 0.001
OSI	10.8 ± 3.31	0.81 ± 0.28	< 0.001
Catalase	9.33 ± 5.05	7.64 ± 3.41	0.185



Frequency of Babesiosis Among Human Who Have Tick Bite History Living in Tatvan Region-Turkey

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Majority of the population deals with agriculture and animal husbandry and intensive rural population in Tatvan region increase risk of biting by ticks. In this study, it has been aimed to research of frequency of babesiosis in humans from Tatvan region by using both Indirect Fluorescent Antibody Technique (IFAT) and direct microscopic examination of thin blood smear preparations. Serum samples have been taken from 100 people who have and 49 people who have not tick biting story from centre of Tatvan and 11 different villages between April-2009 and September-2010. All serum samples have been checked for anti-*Babesia bovis* and anti-*Babesia microti* IgG antibodies by IFAT. In addition, thin blood smear preparations were examined for *Babesia* spp. by direct microscopy.

IgG antibody positivity has been determined at the 18 (12.08%) of the 149 sera against *B. bovis*, 16 (10.73%) *B. microti* and 3 (2.01%) both of them by IFAT. Seropositivity has been determined at the serum samples of 25 (25%) subjects with a history of tick biting and 12 (24.48%) subjects without a history of tick biting. When handles the dispersion according to sex, antibody positivity has been determined at the 11 (16.17%) of the women and 26 (38.23%) of the men. *Babesia* spp. has not been determined at the microscopy. We believe that this study will be the basis of the future epidemiological studies.

Key Words: Babesiosis, Tatvan, Tick, IFAT



Intestinal Microsporidiosis in Immunocompromised Patients from Kayseri-Turkey

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Microsporidia are small, obligate intracellular parasites that infect invertebrate and vertebrate hosts. The infectious stage of a microsporidium is the oval-shaped spore. Spores of species that infect mammals are quite small (1-3 µm). Transmission of microsporidia is believed to occur primarily by fecal-oral, oral-oral or urinary-oral routes. Human microsporidiosis represents an important and rapidly emerging opportunistic disease, occurring mainly, but not exclusively, in severely immunocompromised patients. In this study, *Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* spores were investigated by IFA using monoclonal antibodies which have been directed against spore wall of the microsporidia. A total of 684 immunocompromised patients (398 males, 286 females) who applied to Erciyes University, Medical Faculty, Department of Parasitology were evaluated between November 2009 and March 2011. Of the 684 specimens examined, the microsporidial spores identified were *E. bieneusi* in 27 (3.9%), *E. intestinalis* in 84 (12.3%) and mixed infections in 26 (3.8%). As a result, we believe that immunocompromised patients must be special methods of investigation of these parasites that undetectable by routine stool examination.

Key Words: *Encephalitozoon intestinalis*, *Enterocytozoon bieneusi*, immunocompromised patients, Kayseri



Encephalitozoon Intestinalis: A Report of Two Cases in Both Immunodeficient and Immunocompetent Patients

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Microsporidiosis is an important disease especially in immunodeficient patients; however microsporidiosis are sometimes able to persist and cause chronic infections in immunocompetent individuals. We describe here two cases of intestinal microsporidiosis due to the less common pathogen, *E. intestinalis* in two patients who have different host features.

The first case was admitted to hospital with persistent diarrhea which lasted for 5 months. HIV infection was diagnosed 10 years previously, but he was not under medical follow-up. Antiretroviral therapy was started with a combination of tenofovir/emtricitabine and efavirenz. Stool samples were negative for *Salmonella*, *Shigella*, *Giardia intestinalis* and *Entamoeba histolytica*. PCR of the stool for CMV was also negative. The presence of *E. intestinalis* was confirmed in patient's stool sample by species-specific fluorescing antibodies. The patient was treated with albendazole (400 mg twice daily). After one month therapy diarrhea was completely resolved. The second case was admitted to hospital with nausea, vomiting, diarrhea and severe myalgia. She was working as a physician at a tertiary care hospital and her symptoms started one day before admission. The light microscopy examination of the stool showed several leucocytes. Ciprofloxacin was started. *E. intestinalis* was detected by species-specific FA in stools samples. Her diarrhea disappeared without further treatment. She didn't have any history or finding of immunosuppression and after one year follow-up, she didn't have any gastrointestinal complaints.

This presentation emphasized that the stool samples of the immunocompromised patients should be evaluated for *E. intestinalis* in addition to the routine parasitological examinations.

Key Words: *Encephalitozoon intestinalis*, immunodeficiency, Kayseri



Evaluation of Three Diagnostic Assays for Identification of *Entamoeba histolytica* in Stool Samples

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The intestinal protozoan parasite *Entamoeba histolytica* is responsible for amebic dysentery, colitis, and amebic liver abscess (ALA). The study included 488 patients with diarrhea and 174 asymptomatic subjects. Stool samples from 662 subjects were collected between July 2008 and December 2010 in Turkey. We evaluated performance characteristics of three diagnostic methods (microscopy, enzyme-linked immunosorbent assay (The TechLab *E. histolytica* II ELISA), and real-time PCR for *E. histolytica*. *E. histolytica*/*E. dispar* was found alone in 60 (9.0%) samples by microscopy. The TechLab *E. histolytica* II ELISA was positive in 5.1% (34/662) of stool samples for *E. histolytica*. *E. histolytica* and *E. dispar* were detected in 3.3% (22/662) and 7.5% (50/662) of the stool samples, respectively by real-time PCR. However, no *E. moshkovskii* was detected in any of stool samples by nested PCR. Clinically, diarrhea was mostly prevalent in patients with positive *E. histolytica* real-time PCR assay (20/22), was more prevalent than in those with positive real-time PCR assay for *E. dispar* (27/50). Parasite load can be correlated with clinical outcome in *E. histolytica* infected patients since a parasite load of 103 copy/ μ L and over was detected mostly in patients with diarrhea. These results illustrated that the real-time PCR is a rapid, useful, simple and cost-effective method to simultaneously quantify *E. histolytica* and distinguish it from *E. dispar* in stool samples. Estimating parasitic load can affect the clinical outcome.

This study was supported by a grant of TUBITAK-The Scientific & Technological Research Council of Turkey.

Key Words: *Entamoeba histolytica*, diagnosis, ELISA, real-time PCR



Inactivation of *Cryptosporidium* spp. in Treated Municipal Wastewater and Biosolids by Gamma Irradiation

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Increasing growth of the world's population, waste minimization policies and agricultural needs make the recycling of domestic wastewater quite a desirable practice. Factors like environmental and public health risks must be taken into account when considering treated wastewater for field irrigation and biosolids for land application. Pathogens present in wastewater and biosolids may remain active after treatment and there is always a great risk of transmission of infections via consuming crop and vegetables.

Cryptosporidium spp. is known to be a major cause of human and animal diarrhoea outbreaks as a result of contaminated water supplies. The oocysts' capability of surviving in the environment for long periods of time makes water-borne transmission of *Cryptosporidium* a serious global issue in water safety due to the robust oocyst structure, the small size of this parasite and the low sedimentation rate, conventional water treatment is not totally effective, and oocysts may be present and infective in treated water even if no treatment failure has occurred.

This work represents

- The variations in the population densities of *Cryptosporidium* spp. during a year in treated wastewater effluent and biosolids of Ankara Central Municipal Wastewater Treatment Plant,
- The efficiency of gamma irradiation on the inactivation of *Cryptosporidium* spp.

Key Words: *Cryptosporidium*, gamma irradiation, viability, water



Prevalence of Enterobiasis Among Children in Kyrgyzstan

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Lately in Kyrgyzstan epidemiological situation on parasitic diseases became unsuccessful and it characterizes the country as hyperendemic area. The analysis of epidemic process has been carried out for enterobiasis - the most widespread nematodosis.

For our researches a pilot region was defined with the greatest prevalence of enterobiasis. A rate of infesting by enterobiasis there increased from 0.8% in 2001 to 12.3 % in 2006 per Department of State sanitation and epidemiological surveillance (DSSES) data and in 2009 it was up to 53% per the Sentinel Surveillance data. Our researches show extensive widespread enterobiasis through contact transmission of invasion. In the most cases the disease is registered among children under 14 years old and the average morbidity rate is 4814.7 ± 37 . The highest level of enterobiasis ($54.6 \pm 0.07\%$) is among children under 5 years old. In the age group of 6-14 years is $32 \pm 0.06\%$ ($p < 0.001$).

A characteristic feature of epidemiological enterobioze is nidus. According to our data, the rate of invasion of children attending preschool is significantly higher ($51.9 \pm 0.07\%$) compared with those not enrolled in preschool ($39 \pm 0.06\%$) ($p < 0.001$).

Thus, the spread of enterobiasis in groups of children increases because of hygiene regime violations, over compaction, prolonged stay of large numbers of children in a limited area and high level of contact with source of invasion, which requires the strengthening of sanitary and hygienic regime.

Key Words: Enterobiasis, epidemiology, invasion



Molecular Detection of *Acanthamoeba* spp. in Brackish Water Sediments of Kayseri, Turkey (A Preliminary Study)

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Free-living amoebae (FLA) including *Acanthamoeba* spp., *Naegleria fowleri*, *Balamuthia mandrillaris* and *Sappinia pedata*, are widely found worldwide, and can be isolated from air, soil, and water of natural sources, institutional and domestic water systems. *Acanthamoeba* spp., can cause opportunistic infections such as granulomatous amebic encephalitis and keratitis. This study was aim to investigate the presence of *Acanthamoeba* spp. in brackish water sediments of Kayseri, Turkey.

Water samples were collected in spring 2011 from selected brackish water by immersion of a 50 mL plastic Falcon tube into the upper 2 cm of the water body. Thirteen water samples were examined for evidence of FLA through out the study. The samples were filtrated and transferred to non-nutrient agar plates lawned with *Escherichia coli*, and incubated for 2 weeks at room temperature. FLA was detected both under light and inverted microscopes. DNA extraction was performed using QIAamp DNA Mini Kits (QIAGEN). 229 bp long Nelson f and Nelson r primers used for the PCR. Results for amplification of *Acanthamoeba* DNA by use of PCR with the Nelson primer set were positive for 10 specimens.

This is a preliminary study and further study with more samples is needed in order to confirm the frequency of FLA and to detection of virulence levels.

Key Words: *Acanthamoeba* spp., Brackish water, culture, PCR, Kayseri



A Rare Cause of Diarrhea -*Encephalitozoon intestinalis*- in an Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) Recipient Complicated with Hepatotoxicity After Albendazole Treatment

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A 50 year-old male patient, previously diagnosed with acute myelomonocytic (M4) leukemia in July 2009 underwent allogeneic hematopoietic stem cell transplantation (alloHSCT). In pre-transplant period, complete blood count (CBC), liver and renal function tests, coagulation tests and other parameters were normal. On the first day of transplantation, teicoplanin (400 mg/day for the first 3 days and 400 mg/daily) and caspofungin (first dose 1 x 70 mg/day and 1 x 50 mg/day later) were started intravenously due to white plaques in mouth with oropharyngeal candidiasis and perianal erythema. On the 14th day of the transplantation, watery-diarrhea occurred with abdominal discomfort, nausea and fatigue. His stool examination showed no findings of bleeding. Investigation of microsporidia was confirmed as a rare pathogen -*Encephalitozoon intestinalis*- in patient's stool sample by species-specific IFA and albendazole treatment was started at a dose of 2 x 400 mg/day immediately. On the 5th day of albendazole treatment, (18th day of tx) the liver function tests (LFT) of the patient begun to deteriorate. As LFT continued to deteriorate, albendazole was ceased on the 7th day of treatment. After the biopsy was performed on the 22nd day of transplantation, pathologists confirmed the diagnosis "toxic hepatitis". The LFT began to decrease after ceasing the albendazole treatment. On the 13th day of albendazole treatment period, all LFT values returned to normal ranges. This case shows a rare pathogenic agent -*E. intestinalis*- causing diarrhea in alloHSCT recipient and hepatotoxicity due to albendazole treatment. This is the first reported *E. intestinalis* case diagnosed by IFA from Turkey.

Key Words: Allogeneic hematopoietic stem cell transplantation, hepatotoxicity, *Encephalitozoon intestinalis*, albendazole

INTRODUCTION: Annually, several numbers of aquatic migratory birds migrate from countries placed in northern hemisphere to Mazandaran Province, in the north of Iran, to spend winter season. The objectives of this study were to investigate human cercarial dermatitis (HCD) and determine definitive host in a wildlife refuge, in Mazandaran Province.

MATERIALS and METHODS: This study was conducted on rice farmers in paddy fields from May 2009 to August 2009. To detect HCD cases, the feet and hands of all farmers (n= 1.106) were examined. Clinical signs and symptoms were recorded. Also a total of 260 aquatic migratory birds (mainly *Anatidae* family) were hunted and then nasal mucosa examined for detecting egg, miracidia and or adult worms of birds schistosomes.

RESULTS: Of 1,106 examined subjects, 589 (53.2%) had maculopapular on feet and or hand (mainly on the feet). The majority of cases were adults and were indigenous individuals. Of 260 examined ducks, 41 (15.8 %) were found to be infected with *Trichobilharzia* spp. egg, miracidia or adult worms. The most frequently infected ducks were *Anas clypeata* (79 %) and *Anas platyrhynchos* (18.9%) respectively.

CONCLUSION: Our results showed that cercarial dermatitis and avian schistosomiasis are the most common and most neglected diseases in this area. Moreover, according the high prevalence rate of infection of ducks and high prevalence of HCD in the region; it's considered as a new endemic focus in Mazandaran Province. Also, the results showed that *Anas clypeata* play the most important role in infesting the ponds and paddy fields

Keywords: Avian schistosomiasis, aquatic migrating birds, human cercarial dermatitis, *Trichobilharzia* spp., *Anas clypeata*

Association of Paraoxonase Activity and Atherosclerosis in Patients with *Fasciola hepatica* Infection

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AIM: In this study, our aim was to investigate the association of serum paraoxonase (PON1) activity and atherosclerosis in patients with *Fasciola hepatica* infection.

MATERIALS and METHODS: Twenty two patients with *Fasciola hepatica* and 30 healthy control subjects were included in the this study. We measured the serum PON1, arylesterase (AE), total free sulfhydryl groups (-SH), lipid hydroperoxide (LOOH), oxidative stress index (OSI) and lipid parameters in Fascioliasis and control group.

RESULTS: In all patients, the diagnosis of fascioliasis was made with ELISA test. The ratio numbers of the females to males in patients and the control groups were 19/3 and 25/5 respectively. The mean age was 24.5 ± 18.6 in patients while in control group was 22.2 ± 14.3 years. Regarding age, body mass index and gender, no statistically significant difference was observed between two groups ($p > 0.05$). We showed that PON1, AE, total -SH group and high-density lipoprotein cholesterol (HDL) values were significantly lower in Fascioliasis than controls while the OSI, LOOH and low-density lipoprotein (LDL) values were significantly higher in Fascioliasis than controls. There was statistically significant difference between the patients and control groups for PON1, AE, LOOH, -SH, OSI, HDL and LDL values (Table 1) ($p < 0.05$).

CONCLUSION: We concluded that a decrease in the paraoxonase and arylesterase activities could be explained by an increased in the OSI and LOOH values. The reduced PON1 activities could also contribute to development of atherosclerosis in Fascioliasis.

Key Words: *Fasciola hepatica*, paraoxonase, atherosclerosis

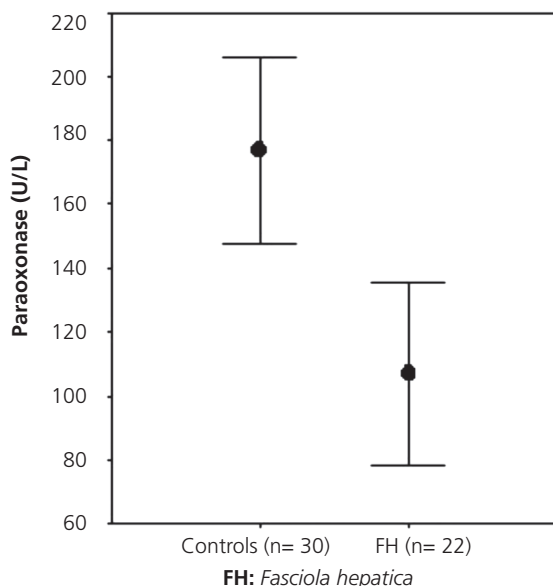


Figure 1. The serum paraoxonase activity of patients and control groups.

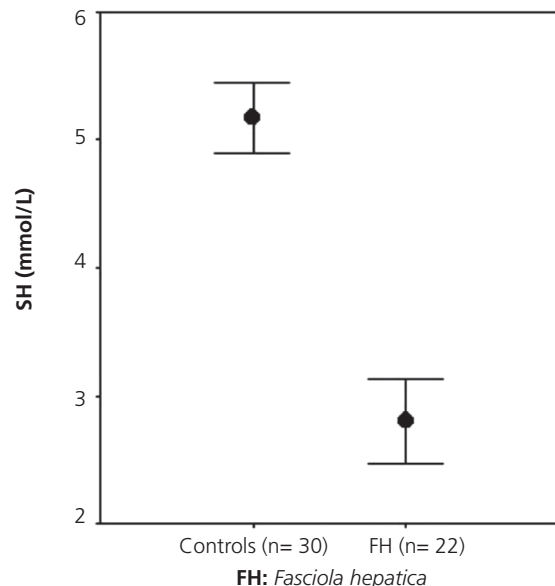


Figure 2. The serum total -SH groups level of patients and control groups.

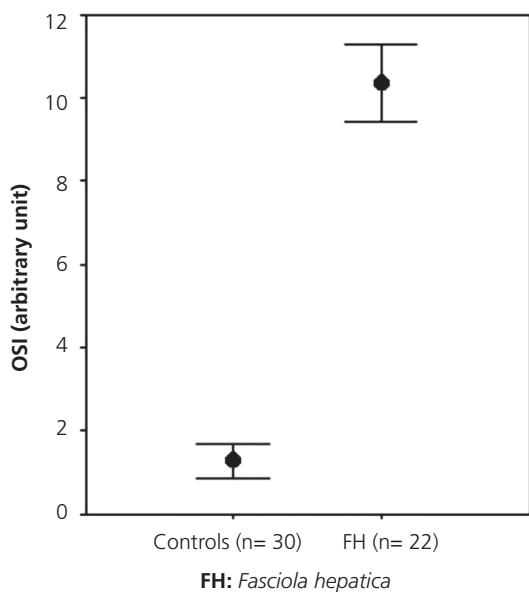


Figure 3. The serum OSI level of patients and control groups.

Table 1. PON1 activity, OSI and other enzymes levels in patients with FH and controls

Parameters	<i>Fasciola hepatica</i> (n= 22)	Control (n= 30)	p
Paraoxonase (U/L)	78.33 ± 27.91	165.17 ± 42.19	< 0.001
Arylesterase (kU/L)	106.76 ± 64.66	176.86 ± 77.69	< 0.001
LOOH (µmol H ₂ O ₂ equiv./L)	99.26 ± 33.67	7.67 ± 5.11	< 0.001
-SH (mmol/L)	0.28 ± 0.07	0.51 ± 0.07	< 0.001
OSI (arbitrary unit)	10.33 ± 2.10	1.28 ± 1.05	< 0.001

LOOH: Lipid hydroperoxide, -SH: Total free sulfhydryl groups, OSI: Oxidative stres index, FH: Fasciola hepatica



Investigation of *Entamoeba histolytica* in Stool Specimens by Direct Microscopic Examination and ELISA in a State Hospital

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OBJECTIVES: Stool antigen assay has been shown to be as sensitive and specific as culture with isoenzyme analysis and to outperform microscopy for the detection of *E. histolytica* in endemic area. Aim of this study is to investigate the presence of *E. histolytica* by ELISA in stool samples.

MATERIALS and METHODS: Between September 2010-May 2011, 975 stool samples of patients of different age groups were sent to microbiology laboratory of Kiziltepe General Hospital. Native-Lugol method and *E. histolytica*-specific antigen test (Adhesin Ag, *Entamoeba* CELISA Path) was applied to all stool samples.

RESULTS: *E. histolytica/dispar* cysts and/or trophozoites were observed in 21 out of 975 (2.2%) stool samples examined by native-lugol. *E. histolytica*-specific antigen in 975 stool specimens was investigated by ELISA. *E. histolytica*-specific antigen was determined in 4 patients which had *E. histolytica/dispar* cysts and/or trophozoites at microscopic examination. Although at direct microscopy of 3 patients *E. histolytica/dispar* cysts and/or trophozoites not observed, *E. histolytica*-specific antigen was found positive. A total of 7 (0.7%) *E. histolytica* specific antigen was found in the patient's stool sample. Patients with *E. histolytica*-specific antigen had been treated.

CONCLUSION: *E. histolytica* specific antigen in stool samples should be investigated to avoid unnecessary treatment.

Key Words: *Entamoeba histolytica/dispar*, specific antigen, ELISA, direct microscopic examination



Generalized Skin Echinococcosis: Case Report

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Echinococcosis of the skin is rarely found, in less than 1%. From our practice we present case of 52 years old patient from Bosnia and Herzegovina, who worked in period 1979-1996 as forester in Schwabian Alps in Germany and was in contact with carcasses of foxes. In 1986 he noticed several secerating round skin changes, as well as lover eyelid skin and in right ear region. Nodules were surgically excised in policlinic setting. Other skin changes were unsuccessfully treated locally with cortisol. In 1991 liver cist was found during CT scan in Germany. The cyst was operatively removed and echinococcosis was confirmed. For the 6 month wound was without healing, and also dissemination of skin changes was noted. Albendazol treatment was conducted, but the skin changes were unchanged. During 1992 two echinococcal cysts on nape were operatively removed with 3 rounds of mebendazol treatment. In 1999, patient was treated again with mebendazole for 7 months without significant effect. In the period 1999-2004 patinet was unreachable and tried a suicide. During 2005/6 with CT scan, intracranial cyst was found, infratentorial.

At clinic for Infectious diseases in Sarajevo patient was treated in 2007 when albendazol therapy was started. Number of skin nodules decreased, except at location of old operative incision despite of albendazol treatment. He was reoperated in 2010. Pathological examination confirmed echinococcosis. Patient is still on albendazol treatment, with stabile psychical condition. In literature we did not find similar case od generalised echinococcosis.

Key Words: Echinococcosis of skin, albendazole, prolonged therapy



Echinococcosis of Paravertebral Muscle as Result of Echinococcosis of the Spinal Vertebra-Case Report

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Human echinococcosis is a parasitic disease of humans and animals that occur throughout the world. The disease can affect any organ, but the most commonly affected organ is liver, then lungs. Echinococcosis of muscle tissue rarely occurs, in about 1 % of cases. The aim of this study was to show the recurring hydatid disease of paravertebral muscles of the region, whose origin was echinococcosis of spinal vertebra. A case of 50-years old worker, whom in May 2007 large echinococcal cyst of the right gluteal region was surgically removed. Two years later, due to pain with flexion, which was identical to earlier preoperative symptoms, CT was performed and revealed a large cystic mass in the right paravertebral muscles. We performed a combined operative drug treatment in plastic surgery with the anthelmintic drug praziquantel. On the MRI image of spine, performed for suspected echinococcosis of bone, changes were found in the fifth lumbar vertebra with spinous process involvement. Postoperatively, the patient is on prolonged albendazole treatment and control of infectious diseases physician and orthopedist.

Key Words: Hydatid, bone, therapy



Paraplaegia Caused with Bone Hydatidosis: A Case Report

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Echinococcosis is antropozoonosis caused by dog tapeworm. Human is secondary host and the disease can affect any organ. Hydatidosis of bone rarely occurs. The first manifestation is usually pain or pathologic fracture. Diagnosis is often delayed, when the disease is already under way. Therapy depends on location and extent of the process. The aim of this study was to point out the consequences that occur if the diagnosis of disease is delayed, and inadequately treated. This paper presents a 50-year-old man who had first operation because of spinal hydatidosis vertebrae thoracolumbalis in age of 27. Later he had five operations because of recurrent echinococcosis. After the fourth surgery, he was motionless, without being able to sit. Last four years he had three fistulas at the back with constantly dripping of clear liquid. In 2004 he underwent a combined operative and anthelmintic drug treatment with praziquantel. Surgeon have found many EC in paravertebral muscles at the area of implanted metal grid which connected the thoracic and lumbal spine (Th-8 to L-1). After healing of the surgical incision the patient was lucky, because he could sit in a wheelchair. There was no fistular activity. He continued physical therapy at the institute for physiotherapy. After three weeks, because od newly formed abscess in the operating section. He was transfered back to the department of orthopedic surgery. Because of the knowledge that he will again need surgery, in a period of mental disorder, he committed suicide.

Key Words: Bone hydatidosis, paraplegia



Isosporiosis in an Elderly Patient With Chronic Diseases: Case Report

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OBJECTIVE: *Isospora belli* is especially common in immunocompromised patients. It is a coccidian protozoon which causes diarrhea that can lead to dehydration frequently associated with watery and secretion-like defecation and requires hospitalization. Clinically, it can cause diarrhea associated with abdominal pain, anorexia, weight loss and abdominal cramps. The laboratory diagnosis depends primarily on the identification of oocysts in stool specimens by direct microscopic examination with iodine or special stains. Trimethoprim-sulfamethoxazole, primethamine and folic acid are the first choice in the treatment. This case is presented in order to draw attention to isosporiosis among the diarrheas that can be seen in the elderly patients with several chronic diseases.

CASE: A 81 year-old debilitated male, who had a history of hypertension, Alzheimer's disease, a surgery of benign prostatic hyperplasia, previous cerebrovascular accident and right hemiplegia, was admitted to our hospital complaining of malaise, anorexia, chills, abdominal pain, disurea, cough, sputum and diarrhea for ten days. In the physical examination, his general condition was moderate and conscious. Laboratory examination revealed decreased levels of hemoglobin, white blood cell, platelet and vitamin B₁₂ and elevated levels of urea, creatinine and INR. Fluid replacement, erythrocyte-platelet suspensions and other treatments were administered to the patient and he was discharged with the recommendations of infectious diseases, hematology and urology outpatients clinic. The patient could submit the stool specimen while he was being discharged. *I. belli* oocysts were detected by the microscopic examination of the sample with iodine after concentration by formalin-ethyl acetate sedimentation. Then, modified acid-fast and trichrome stains were performed and *I. belli* oocysts were detected with both methods. Trimethoprim-sulfamethoxazole was started at a dose of 160/800 mg twice a day for 10 days and he was referred to the outpatient clinic of infectious diseases. But, the patient didn't apply and he died on the second day of the treatment.

CONCLUSION: Similar to this case, infections caused by *I. belli* can be occurred in the elderly immunocompromised patients with several chronic diseases and inadequate nutrition and care. Consequently, in individuals with persistent diarrhea, examinations and tests should be done by taking their immune status into consideration and stool examinations should be done at frequent intervals using the concentrations methods and special stains.

Key Words: Isosporiosis, chronic diseases

Pathogenesis

216-220



Investigation of Oral Microbiological Changes with Removable Orthodontic Appliance Wear

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AIM: The aim of this study was to investigate the oral microbiological changes in children receiving orthodontic treatment with removable appliances.

MATERIALS and METHODS: The sample consisted of 7 subjects (3 females and 4 males). All subjects underwent slow maxillary expansion with the same type of appliance. Two biofilm samples were collected from clasped teeth and hard palate with sterile swabs, the first as a baseline and the second 15 days after appliance wear. Aerobic and anaerobic cultivation performed for each sample. Isolated microorganisms were identified by using conventional biochemical methods and Phoenix 100 (Phoenix 100, BD, Sparks, MD, USA) and API 20A (bioMérieux, Marcy l'Etoile, France) systems.

RESULTS: Gram-positive bacteria such as *Streptococcus oralis* and *Staphylococcus aureus* were isolated from both biofilm cultures. In addition to this, second biofilm culture revealed gram-negative bacteria such as *Pseudomonas aeruginosa*, *Cedecea lapagei*, *Klebsiella pneumoniae* and acid forming gram-positive bacteria such as *Leuconostoc* spp.

CONCLUSION: Removable appliance wear alters the bacterial content of the biofilm which may lead to opportunistic oral infections and an increased rate of dental caries in the absence of good oral hygiene and regular cleaning of the appliance.

Key Words: Microbiological changes, bacteria identification, orthodontic appliance



Quorum Sensing and Virulence of *Pseudomonas aeruginosa* Isolated from Urinary Tract Infections

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In the opportunistic pathogen *Pseudomonas aeruginosa*, the production of several virulence factors such as elastase, rhamnolipids and pyocyanin depends on quorum sensing (QS) involving N-acylhomoserine lactone (AHL) signal molecules. In vitro studies with laboratory reference strains have suggested that the QS system is crucial in the pathogenesis of *P. aeruginosa*. However, there is little known about the importance of *P. aeruginosa* QS systems in vivo.

In this study, to elucidate the contribution of QS systems to the pathogenesis of *P. aeruginosa* during urinary tract infections, we collected 82 clinical isolates obtained from patients at Marmara University Hospital. Isolates were characterized with regard to QS signaling molecules, and virulence factors elastase, rhamnolipid production and biofilm formation. Twelve isolates were found to be negative in the production of either one or both of C12-HSL and C4-HSL QS signaling molecules and at least one of the virulence factors tested.

PCR analysis of these isolates revealed that eight isolates contained all four QS genes while two isolates were negative for *lasR* gene, one isolate was negative for both *rhIR* and *rhII* genes and one isolate negative for *lasI*, *lasR* and *rhIR* genes. Four of eight isolates contained all QS genes were deficient in elastase and rhamnolipid production and biofilm formation. These four isolates contained all four QS genes but lacked all the virulence factors were further analyzed for the presence of mutations. Nucleotide sequence analyses of QS genes of isolates showed that the *lasR*, *lasI*, *rhIR* and *rhII* genes had mutational defects. The combination of *lasR*, *lasI*, *rhIR* and *rhII* mutations probably explains their C12-HSL, C4-HSL and virulence factors deficiencies.

In conclusion, results of this study suggest that naturally QS deficient clinical isolates occur and are still capable of causing clinical infections in humans. The virulence of these QS deficient isolates may be due to the elevated production of either factors that are less stringently controlled by QS or factors yet unidentified.

Key Words: *Pseudomonas aeruginosa*, virulence, quorum sensing



In Vivo Virulence of *Campylobacter jejuni* Exposed to Different Environmental Stresses

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Campylobacter are the most common bacteria causing human gastroenteritis and are mainly transmitted through foods. As foodborne pathogens they have developed survival mechanisms to overcome the stresses they face in the environment and during food processing. However, the link between environmental stress exposure and its virulence properties of *Campylobacter* is not often investigated. The aim of our study was to evaluate the effect of selected environmental stress factors: temperature shift, starvation and atmospheric oxygen exposure on the ability of *Campylobacter* to cause disseminated infection in mice. BALB/c mice were intravenously injected with stressed *Campylobacter* and bacterial invasion into their livers and spleens was followed. At different time points after infection, organs were aseptically removed, dissected and the number of CFU was determined. Simultaneously, paraffin sections were prepared for histopathological evaluation.

According to our results, nutrient insufficiency was the most powerful stress factor which significantly decreased infectious potential of *C. jejuni*, according to the lowest bacterial load in examined organs. Heat shock was also capable to modulate the in vivo virulence of *C. jejuni*, but in a lesser extent than starvation. To the opposite, oxidative stress increased survival of *C. jejuni* inside the livers and spleens of infected mice.

Keywords: *Campylobacter jejuni*, environmental stress, virulence, mice



Cointeractions of *Listeria monocytogenes* and Free-Living Amoeba *Acanthamoeba castellanii*

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Listeria monocytogenes is gram-positive bacterium associated with potentially serious invasive diseases in humans and in a variety of animal species. Because of ubiquitous distribution in the environment, *L. monocytogenes* may be involved in the interactions with free-living protozoa, a common representative of natural ecosystems.

We investigated the interactions of haemolytic *L. monocytogenes* (EGD strain) with the free-living amoeba, *Acanthamoeba castellanii* (ATCC 30234). Survival of bacteria and amoeba was checked at regular intervals, coupled with microscopy.

At 22 °C, as well as at 35 °C, listeria was internalized into *A. castellanii* but was not able to establish an intracellular lifestyle within the eucaryotic host. It was shown, by gentamicin protection assays, that *L. monocytogenes* could be recovered by culture only four hours after coculture establishment. *L. monocytogenes* had no killing effect on the amoebae but did cause rapid protozoan encystment, probably thanks to LLO production. However, the presence of amoeba enhanced the growth of listeria according to higher numbers of extracellular bacteria when cultured with amoebae compared with growth in their absence. Higher numbers were likely sustained on metabolic waste products released during coculture.

Although free-living amoeba and listeria may be found in the same environment it seems that *L. monocytogenes* is not maintained nor transferred in the environment by association with *Acanthamoeba castellanii*. However, presence of acanthamoeba seems to be beneficial for microorganism and it could thus be speculated that such cointeraction is also important for *L. monocytogenes* survival in its natural environment.

Key Words: *Listeria monocytogenes*, *Acanthamoeba castellanii*, coculture, survival



The Levels of Oxidative Stress Biomarkers in Bacteria Homogenates

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PURPOSE: Oxidative stress plays an important role in various infection diseases. The evaluation of oxidative stress biomarkers in bacteria homogenates should be considered a useful data in used therapy. In this study, we aimed to determine oxidative stress biomarkers such as superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) levels in homogenates of various bacteria species.

METHODS: Different species of bacteria (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*) were included in the five samples. The levels of oxidative stress biomarkers (SOD, CAT, MDA) in bacteria homogenates were measured by colorimetric assays.

RESULTS: While MDA level in *A. baumannii* homogenates were found highest in bacteria, it's level in *S. marcescens* homogenates was found lowest. Also MDA levels in *E. faecalis*, *S. aureus* and *S. epidermidis* homogenates were found as similar ($p > 0.05$). Further antioxidant enzyme activities in *S. aureus* homogenates were found higher than the others ($p < 0.05$). The other hand, antioxidant enzyme activities in bacteria homogenates showed significant difference among bacteria ($p < 0.05$).

CONCLUSIONS: We thought that differences in levels of oxidative stress biomarkers in various bacteria homogenates may give information on antibiotic resistance of bacteria and bacterial pathogenicity.

Key Words: Oxidative stress biomarkers, bacteria homogenates

Public Health

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Prevalence of Sexually Transmitted Mixed Chlamydial-Mycoplasmal Infections in High Risk Groups Individuals in Kyrgyz Republic

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OBJECTIVES: The aim of research is to study the prevalence of sexually transmitted mixed chlamydial-mycoplasmal infections in high risk groups in Kyrgyz Republic. Within the framework of our research examined 1868 sex workers (female), 400 intravenous drug users (female) and 2000 females of reproductive age from general population. Individuals of high risk groups were from different parts of Kyrgyz Republic. Particularly patients were from Bishkek, Chuy, Osh, Jalal-Abad and Issyk-kul regions. Detection of infectious agents has been done by direct immunofluorescence, enzyme immunoassay (EIA), polymerase chain reaction (PCR) tests and culture media for *Mycoplasma hominis*.

RESULTS: During the screening of patient's blood for chlamydial and mycoplasmal infections was discovered that the level of mixed chlamydial-mycoplasmal infections in individuals who are practicing risky behavior was- among sex workers 55.2%; 76% in group of intravenous drug users; and in females from general population 9%. It being known that the degree of morbidity by mixed chlamydial-mycoplasmal infections in south parts of Kyrgyz Republic, in Bishkek and Chuy region almost equal, probably it was interrelated with the increase of migration people to capital city and back.

Acute process of mixed sexually transmitted infections was registered among sex workers in 402 patients that composed in 39% and 140 from group of intravenous drug users that composed in 46% of all individuals who have the highest level of specific antibodies to *Chlamydia trachomatis* and *M. hominis*.

CONCLUSION: Consequently among females who are practicing risky behavior in Kyrgyz Republic took place high level of prevalence chlamydial, mycoplasmal and mixed chlamydial-mycoplasmal infections.

Key Words: STD, chlamydial-mycoplasmal infections, sex workers, intravenous drug users



Awareness Level of Biosafety Practices in Dental Profession in Karachi-Pakistan. A Current Status

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INTRODUCTION: The bugs that constitute the microflora in the mouth and nasopharynx and the potential for aerosolization of blood and saliva are high during dental procedures causing serious infections. The objective of this study is to evaluate the level of awareness of dentists with recommended biosafety and infection control procedures that is a part of teaching in dental profession.

METHODS: Undergraduate dental students of different dental colleges and hospitals were selected during 2010. The informed consent obtained from each participant. From a total of 180 students, 72 junior students (38 males and 34 females) and 70 senior students (38 males and 32 females) participated, 142 students complete questionnaire. This study was based on the self applied questionnaire contained 15 closed ended items related to infection control practices. Data analyzed using (SPSS 15.0).

RESULT: The results from this survey were found wearing and changing gloves between patients (99.3%) and face mask wearing was (96.5%), face mask changing between patients (11.3%), changing extraction instruments (88.7%), changing hand pieces (16.3%), changing saliva ejectors (69.5%), changing burs (20.6%) and the rubber dam was used by 29.8% of the subjects, 68.8% subjects disposed sharp objects in a special containers.

CONCLUSION: The potential microorganisms capable of causing serious disease are present in the mouth and saliva of patients who may show no symptoms. Simple infection control precautions, such as use of gloves and a mask and effective hand hygiene practices and mentioned and highlighted above can prevent transmission to dental personnel, their families and their patients.

Key Words: Biosafety, dental, awareness



Emergence of West Nile Virus Infections in Humans in Turkey, August-November 2010

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AIM: To describe the cases and management of West Nile virus (WNV) infections identified in Turkey between August and November 2010.

MATERIALS and METHODS: On 12th of August 2010, Manisa Provincial Health Directorate and Ministry of Health were informed about an increase in the number of hospitalised cases with encephalitis-like-symptoms. According to case definition the blood and CSF samples of suspected cases were sent to the national reference laboratory.

People presenting with fever and meningitis or encephalitis or meningoencephalitis and clear CSF were considered "suspected" and tested for WNV-specific antibodies with ELISA, IFA and confirmed by neutralization (PRNT). A case was considered "probable" if WNV-specific antibody response was demonstrated in his/her serum sample and "confirmed" if PRNT test was positive or specific antibodies were detected in the CSF.

RESULTS: By 2nd of November 2010, 47 cases were detected, 40 with central nervous system manifestations, 7 with non-neuroinvasive symptoms. Of 47 cases, 35 were probable, 12 were confirmed. The patients were from 15 provinces, mainly from the western part of the country. Incidence rate was 0.19/100.000, with the maximum of 1.392 in Sakarya province. Mean age was 58 (Median: 46, range: 4-86). Ten of the patients died. Enhanced surveillance in humans and animals and mosquito control measures were implemented. WNV infection was detected in two horses in Izmir province in September 2010.

CONCLUSION: This is the first time that the WNV infection in humans has been documented in Turkey. Capacity building activities, including surveillance and intersectoral collaboration have been put into practice.

Key Words: Arbovirus, encephalitis, West Nile virus

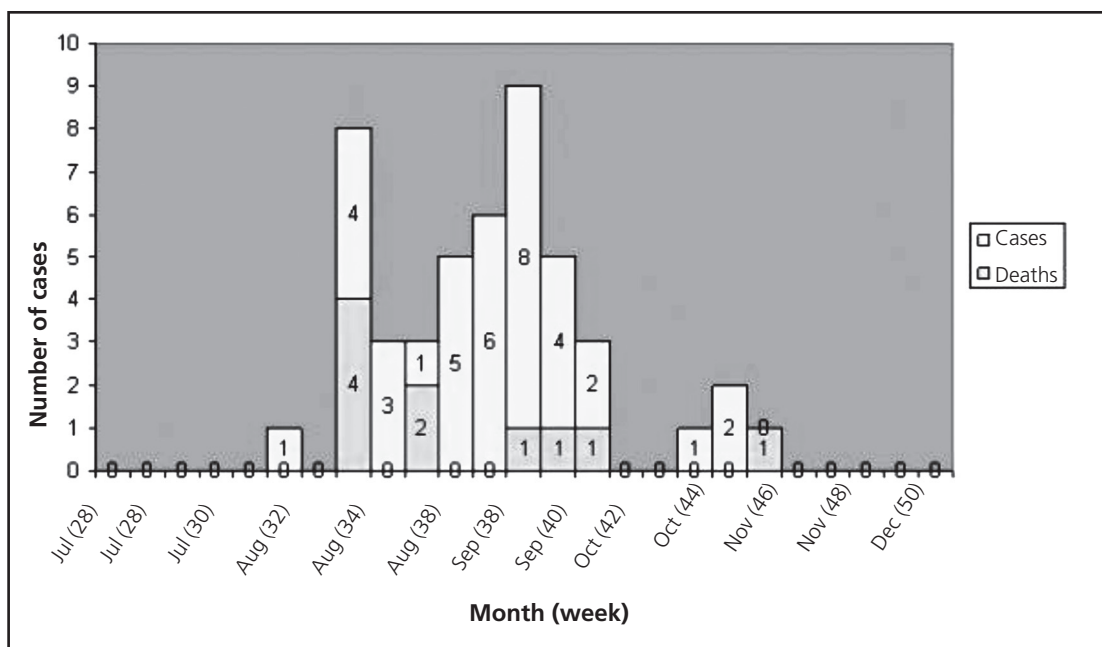


Figure 1. Reported cases of West Nile infection by onset of illness, Turkey, August-November 2010 (n= 47).

Table 1. Characteristics of reported cases of West Nile infections, Turkey, August-November 2010 (n= 47)

Characteristic	Number of cases	Incidence (per 100.000 population)
Age group (years) (n= 46)		
Under 20	8	0.100
20-29	3	0.072
30-39	1	0.026
40-49	6	0.185
50-59	8	0.334
60-69	4	0.278
70-79	11	1.291
80 and over	5	1.632
Total	46	0.19
Province of residence		
Ankara	1	0.021
Adana	1	0.048
Antalya	1	0.052
Kocaeli	1	0.065
Afyon	1	0.142
Konya	3	0.15
Manisa	2	0.15
Izmir	8	0.206
Isparta	1	0.237
Balikesir	3	0.263
Diyarbakir	4	0.264
Aydin	4	0.408
Karaman	1	0.431
Mugla	4	0.498
Sakarya	12	1.392
Total	47	0.19



The Establishment of a Mediterranean Regional Laboratory Network in the Framework of the EpiSouth-Plus Project

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BACKGROUND: The EpiSouth-Plus Project aims at contributing to the control of public health threats in the Mediterranean region and South-East Europe. Twenty-seven countries (9 EU and 17 non-EU, plus one candidate country) currently participate to the Project, which started in October 2010 and will end in April 2013 and is mainly funded by EU DG-SANCO/EAHIC and EuropeAid. One of the Project's work package aims at establishing a Mediterranean Regional Laboratory Network (MRLN) to strengthen the human and technical capacity of participating countries and promote sharing of information to facilitate common threats detection.

METHODS: This activity is co-led by the French Institute Pasteur and the Turkish Refik Saydam National Public Health Agency. A Steering Team composed by representatives of several countries facilitate and enhance the work.

ACTIVITIES and EXPECTED RESULTS:

- Identification of priority areas for common action (pathogens and corresponding diseases) in the Mediterranean basin
- Identification of laboratories interested in joining the MRLN and meeting the expected focus and inclusion criteria
- Links with existing networks
- Mapping of existing biological expertise (Labs and Networks)
- Identification of laboratories' strengths and needs (human, technical and organizational) for diagnosis of priority diseases:
- Regional Laboratories Directory available on the website
- Training (including on-the-job training weeks) and workshops
- Strategic document with recommendations on training and capacity building

CONCLUSIONS: The MRLN will strengthen complementarity among laboratory networks presently operating in the area and overcome national logistic and legislation constraints, in support of the health security preparedness of Europe and Mediterranean.

Key Words: Communicable diseases, health threats, laboratory, Mediterranean region, network



Investigation of Nasopharyngeal Pneumococcal Carriage and Penicillin Resistance in the Nursing Homes and Orphanages

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In general, *Streptococcus pneumoniae* exists in nasopharynx of people. The purpose of this study is to determine, the nasopharyngeal pneumococcal carriage and penicillin resistance in risk groups.

Ninety five people over 60 and 71 children between the ages of 0-12 have been included in the study. In *S. pneumoniae* strains, which are isolated from nasopharyngeal swabs and identified by standard methods, resistance to penicillin has been examined by using oxacillin disk; MIC values have been studied by E-test method in oxacillin-resistant strains.

Nasopharyngeal carriage *S. pneumoniae* has been determined in 7 elderly out of 95 (7.4%) staying in nursing homes, and in 18 children out of 71 (24.4%) staying in orphanages. Four of 7 strains isolated in nursing homes (57.1%), 16 of 18 strains isolated in orphanages (88.9%), have been found resistant to penicillin. In the evaluation of MIC of resistant strains, 2 of 4 resistant strains (50%) in nursing homes have been found susceptible to penicillin, while the 2 strains (50%) have been moderately resistant to penicillin. Twelve of 16 resistant strains (75%) in orphanages have been found susceptible to penicillin, while the 4 strains (25%) have been moderately resistant to penicillin. In the evaluation of MIC in our study we have found no high-level penicillin resistance.

In statistical analyses, connections have been found between pneumococcal carriage and age ($p= 0.03$) and duration of stay in orphanages ($p= 0.03$) in children, while carriage and gender in the elderly. Under these circumstances, penicillin should currently be the drug of first choice in the treatment of pneumococcal infections in our region.

Key Words: Nasopharyngeal carriage, nursing homes, MIC, orphanages, penicillin resistance, *Streptococcus pneumoniae*

Vaccines

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Immune Response of Haemodialysis Patient After Hepatitis B Vaccination

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Hepatitis B presents a significant risk for patients and health care workers in haemodialysis units.

One hundred examiners are divided in two groups, testing and a control group. Testing group was made of 50 examiners on chronic haemodialysis program and the control group was made of 50 examiners: healthcare workers, members of police force and household members of those who are carriers of HBsAg.

The aim of this paper is to establish a titer of anti-HBs in examiners on haemodialysis after hepatitis B vaccination, a titer of anti-HBs in healthcare workers, members of police force and household members of those who are carriers of HBsAg after hepatitis B vaccination and to establish a titer of anti-HBs in examiners on haemodialysis in regards to: sex, age, corpulence, smoking, existence of coinfection with hepatitis C.

It is established that the proportion of non reactors in the control and the test group are statistically very much different. It is established that the proportion of the reactors to vaccine in the examined and control group are statistically very much different. By proportion testing in the test group there was no statistically significant difference between the examiners with normal body weight, and those who are overweight, smokers and non-smokers, males and females, groups of those younger than 50 and those older than 50. It is established that proportions of non-reactors in groups of examiners anti-HCV positive and anti-HCV negative are statistically not very much different.

Key Words: Haemodialysis units, hepatitis B vaccination, titer anti-HBs



Opinions About Vaccination and Observed Side Effects Following Pandemic (H1N1) Influenza A Vaccination in a Training Hospital in Turkey

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The pandemic of influenza A (H1N1) was an important reason of labor and economic losses and caused mortality and morbidity in the season of 2009. The aim of this study was to evaluate the opinions of healthcare workers about influenza vaccination, in a 1100-bed tertiary training hospital in Izmir. A total of 332 healthcare workers were included in the study. Side effects of the vaccine were also monitored. A questionnaire were applied to the vaccinated (n= 247) and unvaccinated (n= 85) groups. Reasons to be vaccinated were advanced age, male gender and having children. The leading causes of accepting vaccination were to prevent transmission within the family (60.3%) and to be in risk group (54.3%). The most important causes of denying vaccination were to afraid of side effects (69.4%) and not to believe the effectiveness of the vaccine (56.4%). Vaccination rates were higher in intensive care units, emergency service and surgery clinics compared to internal medicine clinics. Vaccination rates were higher in cleaning and other paramedical staff compared with health care professionals (doctor, nurse, technician). After vaccination, local reactions were described in a ratio of 43.3% and systemic reactions were described in a ratio of 43.7%. Severe side effects were observed in none of the cases. Worries about safety of the vaccine seems to block vaccination. This condition decreases the effect of our efforts to control of influenza. As a conclusion, data about the safety and side effects of the vaccine should collect, evaluate and regularly report by national influenza surveillance offices.

Key Words: Influenza A virus, H1N1, vaccination, adverse effects



Current Issues of Pneumococcal Disease Among Children in the Republic of Kazakhstan

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One of the major priorities of state policy of the Republic of Kazakhstan up to 2030 is indicated to improve the demographic situation in the country by reducing mortality, including infant and child.

Today all over the world's severe and socially significant burden of pneumococcal disease is recognized. In Kazakhstan in 2008-09 registered annually more than 67,000 cases of pneumonia in children aged 0-5 years of life. Moreover, the incidence of pneumonia among children under 1 year of annual growth to 10% in 2009-rose to 47.1 against 43.6 in 2007. Accordingly, mortality rates for pneumonia among children under 1 year increased from 17.3 to 20.4. So, just for the period 2007-2009 11.374 children died before reaching 12 months of life.

In Kazakhstan, despite advances in the study of etiology, pathogenesis, diagnosis and treatment of respiratory diseases, to achieve significant changes to reduce morbidity and mortality from pneumonia is not yet possible, which requires the study of etiological factors of bronchopulmonary diseases with the use of modern methods of diagnosis.

However, the current economic crisis, one of the most urgent challenges facing governments is the question of optimization of budget spending, while maintaining the achievements in population policy and healthcare. In this connection, according to the decision of the Government of the Republic of Kazakhstan from 2010 to the national immunization schedule introduced vaccination against pneumococcal infections. Even in a phased introduction of vaccination in some areas provides a basis of forecasting major economic and epidemiological effects.

Key Words: Burden, etiology, immunization schedule

Virology

229-250



Evaluation and Comparison of Three Different Anti-Hepatitis C Virus Antibody Tests Based on Chemiluminescence and Enzyme-Linked Immunosorbent Assay Methods Used in the Diagnosis of Hepatitis C Infections in Turkey

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The routine diagnosis of hepatitis C virus (HCV) infection is based on the detection of anti-HCV antibodies by two main methods [enzyme immunoassay (EIA) and chemiluminescence immunoassay (CIA)] but false-positives are a problem. We investigated three anti-HCV tests: two CIAs (Cobas® e 601 and Architect® i2000SR); and one EIA (Ortho® HCV 3.0). Two other anti-HCV tests were also performed as supplementary and confirmatory tests, respectively: a recombinant strip immunoblot assay (RIBA HCV 3.0 SIA) and a reverse transcriptase polymerase chain reaction-based assay for HCV-RNA. After discriminating the false-positive results, the true anti-HCV seropositivity rate in 7156 serum samples was 0.91%. The seropositivity and false-positive rates for the Cobas® e 601, Architect® i2000SR and Ortho® HCV 3.0 anti-HCV tests were 1.9% and 0.99%, 1.2% and 0.29%, and 0.87% and 0.01%, respectively. The mean level of HCV-RNA was 3399×10^3 IU/mL. Critical levels for false-positivity for HCV-RNA were a cut-off index of 200 for Cobas® e 601, a signal/cut-off (S/CO) of 5 for Architect® i2000SR and an S/CO of 1.2 for Ortho® HCV 3.0. Positive and negative results for the RIBA HCV 3.0 SIA assay all accorded with the HCV-RNA assay, except for 23 (17%) indeterminate results, all of which were negative with the HCV-RNA assay. In conclusion, to eliminate doubts related to false-positive findings in the initial HCV screening tests, additional confirmatory HCV-RNA assay should be performed.

Key Words: Hepatitis C virus (HCV) infections, anti-HCV tests, HCV-RNA assay, recombinant immunoblot assay (RIBA), false-positive results



Investigation of the Role of Influenza Viruses A-B, Parainfluenza Viruses 1-3, Respiratory Syncytial Virus and Adenovirus in the Aetiology of Pityriasis Rosea by DNA-Hybridization Method

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Pityriasis rosea (PR) is an acute inflammatory skin disease with unknown aetiology considered to be the most associated with infections. In this study, it was aimed to investigate the role of influenza viruses A-B, parainfluenza viruses 1-3, respiratory syncytial virus (RSV) and adenovirus in the aetiology of PR patients. Thirty out-patients, applying to the dermatology department of Konya Education and Research Hospital, who were diagnosed with PR, and healthy PR negative control group at the same number, age and sex with PR patients were included into the study. In order to enlighten whether an association of PR with the influenza viruses A-B, parainfluenza viruses 1-3, RSV and adenovirus viruses existed or not. RNA materials from influenza viruses A-B, parainfluenza viruses 1-3 and RSV; DNA material from adenovirus were investigated by using DNA reverse-hybridization method in the nasofarengeal samples obtained from patients with PR and control groups included to the study. No RNA positivity was determined, related to influenza viruses A-B, parainfluenza viruses 1-3, RSV and DNA to adenovirus in any of the patients and control groups. As a consequence, viral aetiology of the PR disease still remains unknown, whether to be viral or not, thus further studies are needed to enlighten the unknown aetiology of the disease.

Key Words: Pityriasis rosea, aetiology, viruses, DNA-hybridization



Norovirus and Rotavirus Gastroenteritis in Hospitalized Children, Turkey

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BACKGROUND and AIMS: Enteric viruses (especially rotaviruses and noroviruses) that have been reported as a cause of nonbacterial acute gastroenteritis. This study aims to determine the prevalence and the distribution of viruses responsible for gastroenteritis in children.

METHODS: An epidemiological study on common diarrheal viruses was conducted in Afyonkarahisar, Turkey between January and November 2009. One hundred and fifty faecal samples from children under 6 years of age (mean age, $2.18 \pm SD 3.64$ years, range: 1-72 months) (negative for the presence of pathogenic bacteria by standard culture methods) were tested by ELISA (Ridascreen and Biomeriux) and RTPCR methods for detection of- Norovirus G1, G2. Stool samples positive for group A rotavirus by commercial enzyme immunoassay were subjected to reverse transcription-polymerase chain reaction based genotyping of the outer capsid antigens, VP7 and VP4, determining G and P type specificities, respectively.

RESULTS: Noroviruses were detected in 22.8% of 92 children (< 6 years of age) and rotavirus were detected in 23.3% of 150 hospitalized for gastroenteritis in Afyonkarahisar, Turkey, during 2009; predominant genotypes were GGIb/Hilversum and GGII. 4 Hunter for norovirus. The most common rotavirus strain was G2P[4] (n= 16), followed by G9P[8] (n= 7). Other strains were G1P[8] (n= 3), G2P[8] (n= 3), G1 + 2P[8] (n= 2), G9P[4] (n= 1), G2 + 9P[8] (n= 1), G4 + 9P[6] (n= 1), and G2P[4 + 8] (n= 1). Partially typed strains included 2 G1P[NT] and 3 G2P[NT] strains. Of children with viral enteritis, 6.5% had a mixed norovirus-rotavirus infection.

CONCLUSION: The severity of infection was lower for norovirus than for rotavirus but increased in co-infection.

Key Words: Viral gastroenteritis, rotavirus, norovirus



A Case Report: Herpes Simplex Encephalitis

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INTRODUCTION: Herpes simplex virus (HSV) is a major etiological agent for endemic focal encephalitis. Mortality rate is 70% for un-treated cases. Early diagnosis with appropriate anti-viral medication reduce mortality with a higher percentage.

CASE: A 22 year old woman administered with severe headache/fever within 5 days. She had a loss of consciousness in a mild degree. She presented optic papilla edema/stasis. Thus, a lumbar puncture (LP) was impossible. Vital signs were stable with oral temperature was 39°C. We observed neck stiffness (++++), Kernig sign (+), Brudzinsky sign (+) and bilateral (+) Babinski reflex. Remainder of the physical examination was within normal limits.

Laboratory presented normal leucocyte count and sedimentation. CRP was 57 md/dL.

Magnetic resonance imaging revealed cerebral edema with mild gyral opacifications at inferior/medial segments of temporal lobe and bilateral basal segments of frontal lobe, pointing a HSV encephalitis. We treated by acyclovir (3 x 750 mg intravenously) and mannitol. Afterwards, we observed encephalitis by electroencephalography. HSV IgM and IgG were positive. Medical treatment continued for 21 days. Due to her delayed administration, consciousness returned in 4 days. Patient was discharged with a complete recovery.

CONCLUSION: Early diagnosis and rapid medical treatment among HSV encephalitis cases diminish the incidence of sequelae greatly. A suspicion for HSV encephalitis must be accepted as an indication for a rapid treatment application. Serological parameters may present a delayed positivity. Thus, cerebrospinal fluid evaluation must be applied whenever a LP is possible. If a LP is not possible, MRI and EEG are precious diagnostic tools.

Key Words: Herpes simplex virus, encephalitis



Between the Years 1996-2011 in a Hospital in Istanbul Tagged with Hepatitis D Cases

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In the world 5% of HBV carriers are considered to be infected with HDV. HDV infections whose pathogenicity known to be dependent on HBsAg rarely seen except some areas of Turkey. The number of hepatitis D patients followed in our clinic during last 15 years were 27 (15 male,12 female), two of them hepatitis D superinfection, the other 25 (92%) patients were assessed as co-infection. The age of patients was between 22-63 years, mean age was 37.5. The total number of chronic hepatitis B patients followed during the same period was 1353. According to this, 2% of hepatitis B patients infected with HDV. Twenty three patients were also tested to detect HBV-DNA. The HBV-DNA level was higher than 2000 IU/mL in 4, whereas lower than 2000 in 10 and negative in 9. Only one patient was found to be high viral load (> 1.106 IU/mL). Eight of 27 were found to be positive for HDV-RNA, six negative and 13 of them could not be tested. Concomitant diseases of patients were asthma (n= 1), diabetes (n= 1), brain tumor (n= 1). A patient with acute fulminant course and two other chronic hepatitis D patients, totally three were died because of liver failure. Seven of 12 patients with indication for interferon therapy completed treatment. Despite recommended treatment the other five patients (two of them foreigners) didn't come. One of patients taken IFN alfa for hepatitis B (48 weeks), then IFN alfa for hepatitis D (96 weeks)were cured. Because of side affects, another patient left in the third month of treatment was recovered spontaneously, enzymes decreased to normal values for at least a one-year follow-up, HDV-RNA remained negative.

Key Words: Hepatitis D virus, HBsAg, HDV-RNA, interferon alpha



Detection and Typing of Major HPVs by a New Multiplex Real-Time PCR

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INTRODUCTION: Human papilloma viruses (HPVs) cause of many intraepithelial lesions especially benign hyperplasia in humans. A sub-group of HPVs, that associated with cervical precancerous lesions and cervical cancer, has been called as "high-risk" HPV. Cervical cancer is the the second most frequently occurring cancer worldwide and a major cause of cancer mortality worldwide in womens. Early diagnosis is crucial for prevention and reducing the cervical cancer, and it is depends on greatly the determination of accurate screening strategy. Cervical cytology and HPV-DNA tests are the most commonly used screening methods, for this purpose.

METHODS: A common primer-prob was designed for HPV 6 and 11. Type-specific primers and probes were designed for each of the 14 high-risk HPVs (16, 18, 31, 33, 35, 39, 45, 52, 53, 58, 59, 66, 68 ve 82). Multiplex real-time PCR reactions were carried out in four separate PCR tube with 15 primer pairs.

RESULTS: In total, 51 smear samples were included in this study. A single HPV type was detected in 38 (74,5%) samples, and multiple HPV types were detected in 13 (25.5%) samples. The distribution of genotypes were as follows: HPV-6/11; 13, HPV-16; 23, HPV-52; 11, HPV-18; 6, HPV-68; 4, HPV-58; 3, HPV-31-35-39-82; 2, HPV-33-45; 1.

CONCLUSION: The cervical cancer is declined in developed countries by applied of screening and preventive measures. In this study, we aimed to develop cost-effective, practical and sensitive screening and diagnostic method, and thus to contribute for the reduction of HPV infections and cervical cancer rates.

Key Words: Cervical cancer, HPV, multiplex real time PCR



Comparison of Hepatitis C Virus (HCV) RNA and Anti-HCV Results and Evaluation of the Correlation with Transaminase Levels

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OBJECTIVES: Our aim was to assess HCV RNA and anti-HCV results and their correlation with transaminase levels.

METHODS: A total of 2082 samples collected in last five years were included in the study. Commercial micro and macro ELISA tests were used to detect anti-HCV. Commercial real-time PCR assay was used for qualitative detection of HCV-RNA. Transaminase levels were detected by method.

RESULTS: In this retrospective study a total of 2082 sera from the patients who followed up for hepatitis or suspected to be hepatitis were included to the study. Anti-HCV, HCV-RNA, ALT and AST tests were performed simultaneously. 1551 of the 2082 samples were found positive for anti-HCV. Of the anti-HCV positive patients 763 yielded positive and 788 negative for HCV-RNA. Twenty two anti-HCV negative sera were determined positive for HCV-RNA. When we evaluated liver enzymes of the 1807 serum samples 1192 had normal ALT and AST levels and 615 had elevated ALT and/ or AST levels. Anti-HCV negative, HCV-RNA positive 10 patients had normal ALT and AST levels.

CONCLUSION: As a result patients with suspected hepatitis may have normal ALT and AST results and may have anti-HCV negative results, so molecular methods should be applied especially for the diagnosis of suspected cases although they have no seroconversion.

Key Words: Anti-HCV, HCV-RNA, ALT, AST



An Important Arthropod-Borne Health Problem; West Nile Virus

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West Nile virus (WNV) is a virus of the family flaviviridae which infects people and animals particularly through bites of mosquitos and causes fatal infections characterized by neurologic signs. In the biological cycle of this virus which has a RNA genome, wild birds play an important role along with mosquitoes. WNV infections are observed in many countries in America, Europe, and Asia as well as in Turkey. As of today, there is no vaccine against WNV infections in humans and no effective treatment is known. Infections caused by WNV can be prevented by effective mosquito and wild bird control programs.

Key Words: West Nile virus, mosquito, encephalitis, prevention



Acute HCV Infection as a Result of Artefitial Injury

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Incidence of acute symptomatic HCV infections worldwide is 1-3% or 1 million persons annually. Many cases of acute HCV infections remain asymptomatic and unrecognised. In the paper we presented a case of acute hepatitis C in hospitalised nurse which was punctuated by dirty needle of patient at haemodialysis with chronic hepatitis C two months before admission the hospital. The symptoms of acute HCV infection was appeared 20 days before hospitalisation. First biochemical analyses were shown elevated value of total bilirubin of 4,5 folds and transaminase levels elevated of 17 folds of upper limit of normal range. Between serological markers only a-HBc- At and a-HBs-At were positive like as sign of previous vaccination and, also, HCV IgM-At such as first detected marker of acute HCV infection. PCR detects RNA-HCV of 1.79 x 10⁶ IU/mL, genotip 1a. After the supportive therapy has been ordinated and considerable improvement of biochemical analyses were registered the patient was discharged. Six months later the patient feels good, without symptoms of illness, PCR HCV-RNA was negative, biochemical tests and ultrasound image were normal. In the next period of follow up all tests were stil normal.

Key Words: Artefitial injury, acute HCV infection



The Typhoid Form of Infectious Mononucleosis

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Epstein Barr virus (EBV) is transmitted via intimate contact with body secretions, primarily oropharyngeal secretions. The organism may also be shed from the uterine cervix, implicating the role of genital transmission in some cases. Circulating B cells spread the infection throughout the entire reticular endothelial system. We describe a 21-year-old female student with EBV infection presumably sexually transmitted, presented with symptoms of severe abdominal pain, high fever and jaundice. Abdominal CT scan was performed and showed hepatic, splenic and pancreatic enlargement, and abdominal lymphadenopathy, with signs of layered appearance of a thickened gallbladder wall, minor ascites and pleural effusion. She had no symptoms referable to the oropharynx and did not have lymphadenopathy in other palpable regions. The diagnosis was confirmed with Enzygnost anti-Epstein-Barr virus enzyme-linked immunosorbent assay (ELISA) system.

Key Words: EBV, abdominal lymphadenopathy



Infectious Mononucleosis, 2011

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INTRODUCTION: Mononucleosis syndrome is manifested by abnormality in reticuloendotel system, and etiologically most often caused by EBV, CMV and *Toxoplasma gondii*. Sy IM is manifested in two third of younger nonimmune persons as a result of primary viral infection. EBV is the cause in 90% cases, CMV in 5%, and *T. gondii* in 1% cases and the rest of the cases is caused by different infective agents.

AIM of STUDY: To show the importance of mononucleosis syndrome in modern infective pathology of 21st century.

MATERIALS and METHODS: We retrospectively analyzed clinical characteristic and etiology infective mononucleosis syndrome in the hospitalized patients in Department of Infectious Diseases, RMC Mostar from 2000-2010. There were collected data about sex and age of patients and results of microbiological testing.

RESULTS: In observed period there were hospitalized totally 57 patients with Sy IM, 33 (57,83%) male and 24 (42,10%) female patients with age from 1 to 27 years. In 54 patients (94, 73) as cause of Sy IM was found EBV, CMV in 2 (3.50%), *Toxoplasmosis gondii* in 1 (1.75%), respectively. Clinical manifestations were different. All patients had splenomegaly and lymphadenopathy as main symptoms. Hepatitis was detected in 29% patients (17/57). Complication with the purulent tonsillitis had 77,19% (44/57) patients and two patients developed peritonsillar abscessus. Ampicillin rash had 12, 28% (7/57) patients, and in one patients out of seven rash was manifested as urticaria generalisata.

CONCLUSION: Sy IM is often diagnosed in infectology medicine and is the most often caused by EBV. It manifests as "mild disease", not only in teenagers but in children below 5 and young adults above 20 years.

Key Words: Sy IM, ampicillin rash, incidence, EBV infection



The Epidemiological Situation of Measles in the Republic of Kazakhstan

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We conducted an epidemiological analysis of long-term incidence of measles in the Republic of Kazakhstan for the period 1980-2010. The most intense epidemic of measles were recorded from 1980 to 1984, with an incidence of measles 280.9 per 100 thousand population. In 1988 measles epidemic was reported with an incidence per 100 thousand population-46.0. In 1993 there was a measles epidemic of low intensity with exponent 19.5 per 100 thousand population.

Five years later in 1998, was re-registered with the measles epidemic rate 12.4 per 100 thousand population. The period of vaccination to 1990's was characterized by low-coverage (80%) of children against measles with one dose of vaccine. From 1991 to 1993 the percentage of vaccination coverage of children with one dose of vaccine increased to 90-91.2%. In 2003, measles incidence was 0.16 per 100 thousand population. In the republic in 2004-2005, the epidemic incidence of measles was 106.4 per 100 thousand population. In this epidemic the incidence of measles for children under 1 year was 874.0 per 100 thousand population. In 2005, the Republic of Kazakhstan Ministry of Health organized and conducted national immunization campaigns against measles and rubella, 2.7 million people were vaccinated. The incidence of measles decreased and the epidemiological situation improved. The incidence of measles per 100 thousand population in 2006 was 0.71 in 2007-0.08, in 2008-0.13, in 2009-0, and in 2010-0.02.

Key Words: Epidemiological situation, measles



Situation on Tick-Borne Encephalitis in Kazakhstan

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During last 5 years, 197 confirmed cases of tick-borne encephalitis (TBE) (0.24 ± 0.1 per 100.000 of population) were registered. The epidemic situation has worsened in 2009 when disease growth has made 42.3% (0.3 per 100.000 of population).

The feature of modern TBE epidemiology is a change of disease structure, so 67.3% of patients are non-immunized city dwellers visiting large forests with the different purposes.

The analysis of clinical forms has shown, that the fever form has made 46.9%, meningeal form-30.6%, meningoencephalitis-14.3%, poliomyelitis-8.2%.

In 2009, as a result of favorable climatic conditions, the increase in activity season of Ixodidae ticks till 6 months has been noted. Growth of tick's number has occurred on the majority of endemic territories: in Almaty oblast seasonal number indicator (SNI) of *Ix. persulcatus* was 15.3-54.8 samples per flag/km; *D. marginatus*-2.7-61.6; in the East Kazakhstan oblast SNI of *Ix. persulcatus*-13.9-32.3; *D. marginatus*-12.9-51.2.

According of the previous researches we have observe the change of tick's viraemia: *Ix. persulcatus* - from 16.6-26.0% (1975-1984) to 6.6-7.6% (2003); *D. marginatus*-from 17.7% (1975) to 1.0-1.4% (2003).

It's actual to develop researches on molecular epidemiology of TBE which will lead to formation of new representations about a genetic variety of a virus and geographical distribution of various genetic types.

Key Words: Tick-borne encephalitis, epidemiology, virology, *Ixodidae* ticks

Evaluation of Clinical and Laboratory Predictors of Fatality in Patients with Hantavirus Infection in Turkey

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Hemorrhagic fever with renal syndrome, a serious public health problem in Turkey, is a clinical syndrome that is caused by different Hantavirus types in the family of Bunyaviridae and seen in different regions in Asia and Europe. To determine the clinical and laboratory predictors of fatality among patients with Hantavirus infection.

The present retrospective study was conducted on patients with Hantavirus infection who were hospitalized between March 2010-June 2010 in Burdur State Hospital. Demographic characteristics, clinical findings, and laboratory tests on admission of all patients with Hantavirus infection were investigated. We compared epidemiological, clinical and laboratory findings of the fatal cases with non-fatal cases.

A total of 13 patients with confirmed Hantavirus infection were investigated in this study. Seven (53.8%) patients were female and 6 (46.2%) male. Ages ranged between 11 and 83, with a mean age of 67.3 ± 3.5 in fatal cases and 45.4 ± 20.7 in non-fatal cases ($p > 0.05$). Three of these patients died (23%). White Blood Cell count (WBC), lactate dehydrogenase (LDH), C-reactive protein (CRP) levels, and the international normalized ratio (INR) were higher, hemoglobin (Hb), and platelet counts were lower in fatal cases ($p < 0.05$). The rate of haemorrhage was higher in fatal cases compared with non-fatal cases ($p < 0.05$).

We suggest that for patients with Hantavirus infection who have haemorrhage, elevated WBC, LDH, CRP and INR, and reduced Hb and platelet counts, physicians should be aware of the high fatality risk. These parameters, which can guide the clinician in the prior identification of potentially fatal Hantavirus infection cases, will contribute to the provision of supporting treatment and, when necessary, intensive care services for such patients.

Key Words: Hantavirus, hemorrhagic fever

Table 1. Demographic, clinical and laboratory characteristics of patients with Hantavirus infection

Characteristics	Fatal cases n= 3	Non-fatal cases n= 10	p
Age (years)	67.3 ± 3.5	45.4 ± 20.7	0.104
Sex (male/female)	1/2	5/5	0.563
Duration of complaints until hospitalization, days	2.3 ± 2.3	3.0 ± 1.0	0.671
Fever	2 (66.7%)	8 (80%)	0.580
Myalgia	3 (100%)	6 (60%)	0.497
Headache	2 (66.7%)	8 (80%)	0.580
Exhaustion	3 (100%)	8 (80%)	0.576
Nausea	1 (33.3%)	7 (70%)	0.510
Vomiting	1 (33.3%)	6 (60%)	0.559
Haemorrhage	3 (100%)	1 (10%)	0.014
Laboratory findings			
WBC (μL^{-1})	24.867 ± 1858	10.160 ± 3633	< 0.00001
Hb (g/dL)	10.1 ± 1.1	13.7 ± 1.7	0.006
PLT (μL^{-1})	98.667 ± 71.150	235.900 ± 62.580	0.008
PT (s)	15.2 ± 1.1	14.3 ± 1.4	0.547
aPTT (s)	39.5 ± 5.0	32.2 ± 3.1	0.171
INR	1.4 ± 0.2	1.1 ± 0.2	0.029
AST (U/L)	73.7 ± 42.7	234.6 ± 471.9	0.579
ALT (U/L)	48 ± 47	259 ± 503	0.692
LDH (U/L)	458 ± 94	244 ± 85	0.003
CPK (U/L)	558 ± 670	458 ± 1054	0.881
BUN (mg/dL)	81.3 ± 34.1	14.9 ± 9.2	0.074
Cr (mg/dL)	2.5 ± 2.1	0.9 ± 0.2	0.339
CRP (mg/dL)	21.3 ± 6.7	8.4 ± 6.4	0.014
Total bilirubin	1.0 ± 0.3	1.5 ± 1.9	0.728

Acute Cerebellitis due to Varicella Zoster Infection: Case Report

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OBJECTIVE: To present a case of acute cerebellitis due to varicella zoster infection.

CASE: A 19-year-old man with a five day history of headache, dizziness, ataxia, walking impairment, and dysphasia admitted to our policlinic was hospitalized with suspected cerebellitis. His general condition was middle, conscious, and coopered. Physical examination revealed a 36.5°C/axillary fever, 110/70 mmHg blood pressure, 96/min heart pulse, and disseminate crusted eruptions on the skin (Figure 1). On neurologic examination, nystagmus, ataxia, and romberg positivity were found. From a detailed medical history, the patient was found to have suffered from a varicella zoster infection 10 days previously. Laboratory test results, including white blood cell count, erythrocyte sedimentation rate, C-reactive protein, and blood biochemical parameters were within normal ranges. Lumbar puncture showed a clear appearance, normal protein and cerebrospinal fluid pressure, and 20 lymphocytes/mm³ of cerebrospinal fluid. Brain MRI showed no pathologic lesion. Chest radiograph and abdominal ultrasonography findings were normal. In serological studies, varicella zoster IgM was positive. Acute cerebellitis was diagnosed according to the findings mentioned above. The patient was referred to an infectious disease specialist, and acyclovir treatment was recommended for 14 days, but could not be provided due to limited resources. Instead, symptomatic treatment was administered to the patient for 10 days. The patient made a full recovery with symptomatic treatment alone.

CONCLUSION: Cerebellitis is a rare complication observed after varicella zoster infection. As in the present case, a full recovery from cerebellitis may be made with symptomatic treatment alone.

Key Words: Varicella zoster, cerebellitis, symptomatic treatment



Figure 1. Disseminated crusted eruptions on the skin.



Retrospective Evaluation of Hepatitis E Seropositivity in a Training Hospital in Turkey

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Hepatitis E virus (HEV) which described in 1983 is responsible from hepatitis via enteric transmission especially tropical and sub-tropical areas. Although route of transmission is similar with hepatitis A virus (HAV) infection, HEV infection tend to be fulminant and have poor prognosis in pregnant women. The aim of the study was to evaluate of HEV seropositivity in an 1100-bed tertiary training hospital in Izmir, a city located west of Turkey. Totaly of 653 serum samples collected between 01.01.2008 and 31.08.2010 was included in the study. Micro enzyme immuno-assay (EIA) method (RADIM Diagnostic, Pomezia, ITALY) was used to investigate the presence of anti-HEV IgM and IgG in serum samples. Of the 653 samples, 23 (3.52%) of them were found anti-HEV IgG positive and one (0.15%) of them was found anti-HEV IgM positive. These results were consistent with other studies published in the Aegean region. Although this test is technically easier and cheaper, not taken into routine practice because of the low positivity rate. That is why it is concluded that patient selection should be more selective.

Key Words: Hepatitis E virus, micro enzyme immunoassay



The Frequency of Rotavirus and Enteric Adenovirus in Children with Acute Gastroenteritis in a State Hospital

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OBJECTIVES: Rotavirus and enteric adenoviruses are most important agents cause infectious gastroenteritis. Little is known about the epidemiology of rotavirus and enteric adenovirus gastroenteritis in our location. In this study, it was purposed to determine the epidemiology of rotavirus and enteric adenovirus gastroenteritis among pediatric patients in Kiziltepe General Hospital.

MATERIALS and METHODS: The epidemiological data of gastroenteritis caused by rotavirus and adenovirus was reviewed retrospectively. In total, 426 pediatric patients admitted between May 2010 and March 2011 was diagnosed as acute gastroenteritis. Rotavirus and enteric adenovirus antigens were examined in the fresh stool specimens with Immuno-chromatographic fast assay (RIDA, QuickRota-Adeno-CombiR-Biopharm AG, Germany).

RESULTS: 8 cases (1.9%), adenovirus, 40 patients (9.4%), rotavirus, in 10 cases (2.3%) were positive with the rotavirus and adenovirus. The high-positive-rate were found in for rotavirus October (30%), November (40.8%), December (14.9%), January (13%). The highest positive rate of adenovirus were determined in May (9.5%) and July (10%), August (7.4%), October (10%). The lowest rate of rotavirus-positive were found in the months of September (0%) in May (0.2%), and June (0.2%), July (0.2%), respectively. Adenovirus had the lowest positive rate in September (0%), December (2.1%), January (2.2%), March (2.9%). Viral antigen-positive cases, was observed in autumn and winter months with most common 0-2 months age-group.

CONCLUSION: Rotavirus is most important agent in acute gastroenteritis in childhood. It should be investigated routinely in fresh stool specimens, especially in the autumn and winter months.

Key Words: Rotavirus, enteric adenovirus, gastroenteritis, children

Efficacy and Safety of Entecavir Treatment in HBeAg Positive Patients with Chronic Hepatitis B

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BACKGROUND: This study reports retrospectively the 96 week long-term efficacy and safety data with entecavir treatment in nucleosid(t)e-naive 49 HBeAg-positive CHB patients with various baseline.

METHODS: This is a multicenter study from Southeast part of Anatolian of Turkey (Diyarbakir, Batman, Kiziltepe and Midyat) between 2007-2009. Forty-nine HBeAg-positive patients who had never taken nucleosid(t)e treatment received entecavir therapy. All patients has increased serum alanine aminotransferase (ALT) level. Serum HBV-DNA load was measured with quantitative real-time PCR. Statistical analyses were performed with the Statistical Package for Social Sciences version 15.0 software.

RESULTS: Forty-nine adults between 22 and 60 years of age was enrolled. The initial mean values of ALT was 79.4 ± 41.5 IU/L. At the baseline, mean of fibrosis score of liver biopsie was 2.27 ± 0.75 . 8.2% patients achieved HBV DNA < 300 copy at the week 12 of the treatment, 89.8% at the week 48 and 91.7% at the week 96. HBeAg loss was observed in 7.1% of the patients on treatment at week 96. HBeAg seroconversion were observed in 4.8% patients on treatment at week 96. HBsAg seroconversion was observed in 2.1% of patients on treatment at week 96. Safety through treatment was good. No patient had a confirmed creatinine increase of 0.5 mg/dL. Renal safety was good.

CONCLUSION: Entecavir was well tolerated and produced potent, continuous viral suppression with increasing HBeAg loss through week 96. The safety profile was good, and there is no evidence of virological breakthrough under the treatment with entecavir.

Key Words: Chronic hepatitis B, treatment, entecavir, efficacy, safety

Table 1. Results of entecavir treatment at the 96 week

		96 Week HBV-DNA > 300 Copy/mL			HBeAg loss		
		n	%	P	n	%	P
Age	< 40	28	100	0.025	3	10.7	0.255
	≥ 40	16	80		0	0	
Gender	Female	18	90	1.000	3	15.0	0.066
	Male	26	92.9		0		
Fibrosis	< 3	26	86.7	0.290	2	6.7	1.000
	≥ 3	14	100		1	7.1	
HAI	< 7	26	92.9	0.614	1	3.6	0.543
	≥ 7	14	87.5		2	12.5	
Baseline ALT	< 70	11	73.3	0.007	0	0	0.542
	> 70	33	100		3	9.1	



The Seroprevalence of Hepatitis B Surface Antigen (HBsAg) in Pregnant Women in Batman

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OBJECTIVES: To investigate the seroprevalence of HBsAg among pregnant women in Southeastern Anatolia region of Turkey, city of Batman.

MATERIALS and METHODS: In this retrospective study 15.585 pregnant women who attended to the Obstetrics and Gynecology department of Batman Maternity Hospital between April 2008 and December 2010 were tested for hepatitis B surface antigen (HBsAg) by Enzyme-Linked Immunosorbent Assay (ELISA) method. Babies of mothers with HBV infection were tested for HBsAg at about 9 months of age.

RESULTS: Out of 15.585 pregnant women, 668 (4.2%) were found HBsAg positive. Their mean \pm SD age was 30.13 \pm 6.58 years. Hepatitis B was detected in 137 (20.5%) babies born to mothers with HBV infection.

CONCLUSION: In our study the seroprevalence of hepatitis B in pregnant women are similar to the rate of that were reported in other studies in Southeastern Anatolia region of Turkey.

Key Words: Hepatitis B, pregnant women, seroprevalence



Rapid Identification of 12 Respiratory Viruses Using a Dual Priming Oligonucleotide System-Based Multiplex PCR Assay

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OBJECTIVES: Rapid and accurate diagnosis of viral respiratory infections is important for providing timely therapeutic interventions. This study evaluated a new multiplex PCR assay (Seegene Inc., Seoul, Korea) for simultaneous detection and identification of 12 respiratory viruses using two primer mixes. The viruses included parainfluenza viruses 1, 2, and 3, human metapneumovirus, human coronavirus 229E/NL63 and OC43, adenovirus, influenza viruses A and B, human respiratory syncytial viruses (RSV) A and B, and human rhinovirus A. The aim of the study is to describe the epidemiological and clinical characteristics of acute viral respiratory infection in hospitalised Turkish children and few adults, Afyonkarahisar/Turkey.

METHODS: One hundred-seventy patient samples (nasopharyngeal swabs) were collected with flocked swabs and transported in UTM (Copan diagnostics) from November 2009 to May 2010. These frezed to 20 C before being shipped on dry ice for batch testing. Some of the samples tested with the QuickVue[®] influenza A + B flu Dipstick in terms of A and B. mRT-PCRs for the detection of 12 respiratory viruses (Seeplex[®] RV detection kit, SeeGene, Seoul, Korea) were tested with frozen specimens.

RESULTS: mRT-PCR detected causative viruses in 39 (22.9%) patients, including 3 co-infected cases. A total of 39 viruses were identified: RSV A/B (8.2%/4.7%), influenza virus A/B (1%), human metapneumovirus (0.6%), adenovirus- RSV B (1%), rhinovirus (6.5%), and coronavirus OC43 (1.8%). One of influenza A, confirmed as H1N1 in the reference laboratory later.

CONCLUSION: DPO-based mRT-PCR was found as a rapid and sensitive tool for the detection of the viruses that cause childhood respiratory infections.

Key Words: Viral respiratory infections, mRT-PCR, Seegene



Hematological Manifestations in Patients with Crimean-Congo Hemorrhagic Fever

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BACKGROUND: Crimean-Congo hemorrhagic fever (CCHF) is a viral hemorrhagic syndrome presenting with fever, nausea, vomiting, myalgia, hematological changes and bleeding from various sites. In this study investigated the hematological changes in patients with CCHF.

MATERIALS and METHODS: We retrospectively analyzed demographic, clinical and laboratory characteristics of patients with CCHF.

RESULTS: A total of 152 patients with confirmed CCHF were investigated. Bleeding was observed in 63 (41.4%) patients. Patients exhibited hemorrhagic signs including epistaxis (25.7%), gingival bleeding (13.2%), ecchymosis (11.8%), melena (10.5%), hematemesis (7.9%), hematuria (7.2%) and vaginal bleeding (6.6%). Thrombocytopenia developed in 137 (90.1%) patients, while platelet counts were below 50.000/mm³ in 31.6% of CCHF patients. Leucopenia was present in 88.2% of patients and anemia in 13.2%. Prolonged activated partial thromboplastin time (aPTT) was present in 47.4% of patients, prolonged prothrombin time (PT), in 21.1%, and high international normalized ratio (INR) in 25.7%. Disseminated intravascular coagulation (DIC) developed in 17.8% of cases. Hemophagocytosis was determined in 35.9% of patients subjected to bone marrow aspiration. Ten (6.6%) patients died.

CONCLUSIONS: Hematological changes such as thrombocytopenia, leucopenia, prolonged PT-aPTT, high INR and DIC are observed in patients with CCHF, a viral disease that follows a hemorrhagic course. CCHF patients' hematological parameters must therefore be closely monitored and the necessary measures taken in good time.

Key Words: Crimean-Congo hemorrhagic fever, CCHF, hematological manifestations, hemophagocytosis



An Analysis of Risk Factors for Fatality in Pandemic Influenza A (H1N1) Virus Infected Patients

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This study was intended to determine predictive fatality criteria based on clinical and laboratory findings at admission to hospital of patients diagnosed with pandemic influenza A (H1N1) virus infection. Ten (20%) of the 50 patients included in the study died. Average age of the fatal cases (48.8 ± 16.5) was significantly higher than that of the survivors (34.5 ± 18.4). No significant difference was observed between the groups in terms of underlying chronic diseases and pregnancy. Fever, phlegm, shortness of breath, tachypnea and cyanosis were observed at significantly higher levels in fatal cases. Serum hemoglobin (Hb), glucose and albumin levels and arterial oxygen saturation (SaO₂) were significantly lower in fatal cases compared to survivors; serum aspartate transaminase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), C-reactive protein (CRP) and procalcitonin (PCT) levels and time between onset of symptoms and commencement of antiviral treatment were all significantly higher in fatal cases. Clinical and laboratory parameters with a high negative predictivity for fatality were, in order, time between onset of symptoms and commencement of antiviral treatment, serum albumin level, days of hospitalization, serum glucose, CRP, patient age and serum BUN level. The parameters with the highest positive predictive value were SaO₂, serum lactate dehydrogenase, serum albumin levels and days of hospitalization. This study shows that in addition to demographic characteristics and clinical findings, prognosis of patients with pandemic influenza A (H1N1) virus infection can be determined before hand with various laboratory tests. But these parameters, which can guide the clinician in the prior identification of potentially fatal pandemic influenza A (H1N1) cases will contribute to the provision of supporting treatment and, when necessary, intensive care services for such patients.

Key Words: Pandemic influenza A (H1N1) virus, treatment, prognosis, predictive factors



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