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**Topics in Infectious
and Tropical Diseases**

new Microbiologica Proceedings

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March 12-13, 2009

**National Museum of Science
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Program

Thursday, March 12

07.45 **Registration of Participants**

Opening remarks

08.45 **Message from the President of the Congress**

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Antibiotic resistant pathogens and infections transmission

Chairpersons: G. Cornaglia (*Verona*), G. Fortina (*Novara*)

Keynote Lecture

- 09.15 • **Clostridium difficile infection: a worldwide spreading epidemic**
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- 09.45 • **Gram negative emerging pathogens in Italy: the role of Microbiology Laboratory**
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- 11.15 • **High resistance emerging strains in Long Term Care Facilities in Italy: epidemiological and microbiological patterns**
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Chairpersons: G. Gesu (*Milan*), S. Esposito (*Naples*)

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IL SALUTO DEL PRESIDENTE

Illustri ospiti, carissimi colleghi ed amici, siamo arrivati alla seconda edizione del Congresso AMIT ed anche questa volta non possiamo nascondere l'emozione e la soddisfazione di avere proposto un evento che offre un insieme di argomenti di grande attualità nel campo della cultura delle infezioni attraverso una visione di insieme che ne considera tutti gli aspetti: infettivologico, microbiologico, igienistico e legale.

Gli argomenti di questa edizione sono stati da noi scelti sulla base delle situazioni o meglio delle emergenze di chi lavora in questo campo e deve affrontare quotidianamente con grandi competenze professionali patogeni sempre più resistenti che determinano un aumento del rischio di contrarre infezioni e, in alcuni casi, possono indurre delle vere e proprie emergenze epidemiche o, addirittura, endemiche. Le emergenze infettive differiscono profondamente dalle forme croniche sia infettive o degenerative: infatti il controllo di quest'ultime è ormai legato a farmaci che devono essere somministrati per tutta la vita come nelle infezioni da HIV o per lunghi periodi come nella tubercolosi; le patologie acute batteriche necessitano di interventi immediati (diagnostici, terapeutici, di prevenzione) che se non effettuati in poche ore o addirittura in pochi minuti, possono esitare in gravi conseguenze per il paziente e la comunità.

Riteniamo, a tal proposito, che la patologia infettiva dell'anziano in continuità assistenziale sia un tema molto sentito dai clinici di varie discipline e che lo si debba affrontare in tutti i suoi aspetti. All'estero si è sviluppata una vera e propria cultura scientifica dedicata e vi sono numerosi team che se ne occupano da tempo; in Italia vi sono solo poche esperienze in merito e noi crediamo che sia il momento di diventare protagonisti attivi in quanto abbiamo una grande e storica tradizione di tutela delle persone più deboli e più a rischio come appunto l'anziano.

È necessario fare il punto sulla terapia antibiotica in un contesto economico-sociale molto difficile per la ricerca farmacologia di base che è in sofferenza e dove le scelte di molte aziende sono maggiormente orientate nello sviluppo di molecole di altro tipo; in tale situazione il nostro armamentario terapeutico diventa così sempre più esiguo mentre servirebbero maggiori opzioni proprio per la sempre più diffusa antibiotico resistenza.

Altro cardine della gestione delle infezioni è la prevenzione: siamo infatti sempre più convinti che chi si occupa di questi problemi debba organizzare il proprio lavoro non solo dal punto di vista diagnostico-terapeutico ma anche di prevenzione mettendo insieme competenze professionali diverse ma tutte indirizzate allo stesso fine.

Abbiamo pertanto voluto dedicare più di una sessione congressuale a tali temi di grande attualità: la gestione dei dispositivi protesici e la corretta applicazione dei protocolli in uso nei trapianti d'organo; abbiamo cercato di mettere a confronto l'organizzazione di due sistemi sanitari per il controllo delle infezioni: quello francese, all'avanguardia in Europa, ed il nostro che ha fatto notevoli progressi negli ultimi anni ma che necessita di una maggiore integrazione tra le diverse realtà regionali.

Non possiamo poi chiudere gli occhi di fronte al susseguirsi di notizie da tutte le regioni italiane di procedimenti amministrativi o penali che vedono coinvolti sanitari che operano nel campo del controllo delle infezioni. A volte si confonde un fenomeno sempre più diffuso come quello dell'aumento di ceppi batterici più resistenti ed aggressivi sia in ospedale che nel territorio con responsabilità individuali o collettive: auspichiamo che vengano presi al più presto provvedimenti legislativi a tal proposito per evitare lunghissimi e penosi contenziosi tipo "processi agli untori" che, tra altro, determinano un incongruo e costoso aumento di prestazioni dovute alla cosiddetta "medicina difensiva".

In ultimo, abbiamo dedicato uno spazio alle potenzialità immuno-terapeutiche nel campo dell'infezione/malattia da HIV, nella speranza che si avvicinino sempre di più all'impiego clinico ed alla nuova frontiera dell'immunogenetica che è diventata ormai non solo una realtà consolidata nelle scelte diagnostiche del clinico ma, in alcuni casi, obbligatoria.

Il nostro Congresso è stato realizzato solo grazie ad una grandissima collaborazione tra l'organizzazione e molte Aziende Farmaceutiche che, ancora una volta, hanno creduto di poter investire in una cultura scientifica e divulgativa dimostrando come, anche in momenti di grande crisi economica come l'attuale, sia necessario guardare avanti ed avere fiducia nel progresso della medicina e del welfare.

Il livello scientifico di un Congresso e quindi la sua riuscita finale deriva da chi porta contributi scientifici ad alto livello: noi crediamo che tutti i relatori e moderatori italiani e stranieri (che ringraziamo particolarmente) presenti tra noi rappresentano davvero l'eccellenza in campo scientifico.

Ringraziamo tutti i rappresentanti delle istituzioni che, numerosi, ci hanno anch'essi onorato della loro presenza sia in aula che nelle sessioni congressuali e che siamo certi non faranno mancare in futuro il loro appoggio a chi vive le difficoltà di tutti i giorni e dovrà presto affrontare in futuro sfide sempre più impegnative.

Un messaggio di gratitudine va all'Agenzia Nadirex che ci ha ancora supportato per ottimizzare al meglio l'organizzazione.

Non possiamo dimenticare i medici ed il personale infermieristico dell'U.O di Malattie Infettive e Tropicali dell'Azienda Ospedaliera di Lodi che in silenzio ed con grande abnegazione hanno anch'essi dato un valido contributo alla realizzazione di questo evento.

Non vogliamo dilungarci ancora perché il tempo preferiamo dedicarlo alle sessioni scientifiche ma non possiamo fare a meno di sperare che il nostro sforzo possa servire a rendere più saldo il sistema salute del nostro paese anche in momenti difficili come quello che stiamo vivendo. È proprio in queste contingenze che il nostro spirito di sacrificio ed abnegazione vince sempre e comunque sulle avversità. Grazie di cuore di essere qui con noi così numerosi.

Dichiaro aperti i lavori

Marco Tinelli

GRAM-NEGATIVE PATHOGENS EMERGING IN ITALY

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Since recent years Gram-negative pathogens are back as major players in the clinical setting, thanks to the emergence of powerful resistance determinants that allow them to escape the lethal action of the most recent and potent anti-Gram-negative antibiotics such as expanded-spectrum cephalosporins, carbapenems and fluoroquinolones.

In fact, several beta-lactamases of various groups (extended-spectrum beta-lactamases [ESBLs], AmpC-type beta-lactamases and carbapenemases) have emerged in members of the family *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, and are typically found in multidrug-resistant (MDR) strains of the above species. On the other hand, the dissemination of transferable fluoroquinolone resistance genes (e. g. *qnr*, *aac-cr*) is thought to provide a major contribution to the increasing fluoroquinolone resistance rates recently observed among *Escherichia coli*, *Klebsiella pneumoniae* and other *Enterobacteriaceae*.

In the Italian scenario, MDR *Enterobacteriaceae* producing ESBLs are widespread, not only in acute-care hospitals but also in long-term care facilities which represent an important reservoir for such MDR pathogens, and represent one of the major resistance challenges. Massive dissemination of the CTX-M-type ESBLs has recently been observed also in our country, where it has contributed to a rapid and remarkable modification of the ESBL epidemiology, similar to that observed in other European countries. *Proteus mirabilis* resistant to third-generation cephalosporins, producing AmpC-type beta-lactamases, is another emerging resistance issue in Italy. Finally, the dissemination of metallo-beta-lactamases (MBLs) in *P. aeruginosa* and of OXA-type carbapenemases in *A. baumannii* has resulted in the emergence of several clones of those pathogens which exhibit extended-drug resistance phenotypes that include most of the available antimicrobial agents.

This presentation will focus at the recent epidemiological evolution of MDR Gram-negatives observed in Italy, and will discuss the challenges encountered in the Clinical Microbiology laboratory for a correct identification and reporting of these pathogens, which is crucial not only to targeted antimicrobial therapy but also for surveillance and infection control purposes.

EMERGING GRAM-POSITIVE PATHOGENS IN ITALY: CONTRIBUTION OF MICROBIOLOGY TO INFECTION DIAGNOSIS

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According to the CDC of Atlanta, emerging infections include not only those caused by newly-described human pathogens but also those that are occurring with increasing frequency, or that are associated with more serious clinical manifestations, in new patient populations or geographic areas. Contribution to infection emergence is due to host-specific, pathogen-specific and environmental factors. Effective infection treatment and infection control efforts depend on the performance of the laboratory to detect the emerging pathogens accurately, including their antibiotic-resistance patterns and the presence of particular virulence factors responsible for increased pathogenicity or transmissibility.

Gram-positive bacteria are a phylogenetically diverse group of microorganisms that are involved in a variety of serious infections. The last decade of the past century has witnessed the emergence and world-wide spread of Gram-positives as major antibiotic-resistant pathogens: typical examples are penicillin-resistant *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant Enterococci (VRE). According to data from the European Antibiotic Resistance Surveillance System (EARSS), in Italy the prevalence of MRSA and VRE appears to be slowly decreasing although it is still high if compared with that of other European countries. The rate of MRSA among *S. aureus* blood isolates is currently 34% and the rate of VRE among *E. faecium* blood isolates is 11% (1). Penicillin-resistant *S. pneumoniae* is not a major problem in Italy and the availability of a pediatric vaccine against 7 common serotypes is contributing to the reduction in the number of invasive infections among children.

Although conventional methods still remain the principal approach for detection and identification of pathogenic bacteria and their resistance patterns, methods based on molecular technologies have contributed significantly to the detection of emerging Gram-positive infections and their characterization. Molecular assays for resistance markers are very reliable: detection of the type of *van* gene carried by VRE or the presence of *mecA* in MRSA can be accomplished rapidly and precisely by PCR. In addition, molecular methods have provided a major contribution towards the understanding of the spread of particular clones and of the nature of new types of infections. One important example is provided by the emergence of community-acquired (CA)-MRSA. Although MRSA has been considered for decades a typical nosocomial pathogen, causing infections in high-risk patients, in the past decade this versatile microorganism has evolved into a major cause of community-acquired infections. New lineages of MRSA, defined community acquired (CA)-MRSA, with peculiar microbiological characteristics and a special propensity to cause infections in young individuals in the community, have emerged. While in the USA,

CA-MRSA strains belong to a single widespread clone, designated USA300, in Europe they belong to a variety of different clones. Most strains carry the genes for a characteristic toxin, the Panton-Valentine leukocidin (PVL), whose role in disease is still a matter of debate. In Italy, a few serious infections due to typical CA-MRSA have been recognized including necrotizing pneumonia, meningitis, bacteremia and skin and soft tissue infections. These serious infections were caused by MRSA belonging to different clones: ST80 (the European clone) ST8 (USA300), ST30 (the Southwest-Pacific clone) and others. In our experience, these typical CA-MRSA causing serious infections are consistently PVL-positive. An unexpected finding is the occurrence of serious community-acquired infections due to strains of *S. aureus* that are methicillin susceptible (MSSA) but carry the PVL genes. These infections have striking similarity with those due to CA-MRSA; we have recently described a large and prolonged outbreak of skin infections caused by a PVL-positive MSSA strain, that was probably initiated in the maternity ward of the local hospital and subsequently spread to the community causing familial clusters of infections (2).

Attention to the community has been further attracted by the view that MRSA infection can be a zoonosis. Pigs represent a large reservoir of MRSA and individuals professionally exposed to pigs, such as farmers and veterinarians, can be colonized and infected. The pig MRSA lineage does not usually contain the PVL genes and can be identified only on the basis of molecular markers such as non-typability by PFGE and ST398. Two cases of serious soft tissue infections due to ST398 MRSA have recently occurred in Italy in professionally exposed individuals.

Among serious Gram-positive infections emerging in Italy we have to mention *Streptococcus suis* meningitis, and *Corynebacterium striatum* infections. *S. suis* is an emerging human pathogen that is acquired through contaminated pigs or pig meat. Two cases have been described in Italy in the past 2 years (3) but the disease is probably underreported because the causative agent is easily misidentified. *C. striatum* is an important cause of bacteremia and ventilator-associated pneumonia in Intensive Care Unit patients as shown by a collaborative study involving different Italian clinical centers (4). In both these studies, molecular methods have been instrumental to the diagnosis of the infection and the confirmation of the susceptibility patterns.

Increased awareness of both clinicians and microbiologists is needed to evaluate the full extent of the burden of emerging Gram-positive infections in Italy and the impact of antibiotic-resistant patterns on treatment.

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INFECTIONS OF THE ELDERLY IN LONG TERM CARE FACILITIES: NEW CHALLENGES TO FACE?

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Occurrence of infection

Infections are common in residents of long term care facilities. The most frequent endemic infections are pneumonia, urinary tract, skin and soft tissue, and gastrointestinal infections (1). Pneumonia has a mortality of 10-25%, but is the only infection which contributes substantially to mortality. Outbreaks of infection are frequent, usually due to respiratory or gastrointestinal viruses. Some facilities also have a high prevalence of resident colonization with resistant organisms such as methicillin-resistant *Staphylococcus aureus*, vancomycin resistant enterococci, and extended-spectrum beta-lactamase producing Enterobacteriaceae.

Factors contributing to infection

Normal aging changes may promote infection. The decline in T cell function with immunologic aging leads to reactivation of latent infections such as tuberculosis and varicella zoster virus (shingles). All organ systems experience alterations with aging which promote infection. For instance, the risk for and severity of infection is increased by the decreased cough reflex and decreased mucociliary clearance of the aging respiratory tract, or the thinning and delayed healing of the aging skin.

Resident comorbidities also increase the risk of infection. Neurologic diseases impair mobility, increasing the risk of pressure ulcers, and may impair swallowing, leading to aspiration and respiratory tract infection. Prostatic hypertrophy in men is associated with an increased risk of urinary tract infection. Pedal edema secondary to congestive heart failure or venous insufficiency is a risk for erysipelas. Functional impairment is also an independent risk factor for infection. Medications and other interventions for resident care also facilitate infection. H2 blockers and proton pump inhibitors, for instance, decrease gastric acidity and increase the risk of gastrointestinal infections. Invasive devices including indwelling urethral catheters, percutaneous feeding tubes, tracheostomies, and central vascular lines are all associated with an increased risk of infection attributable to the device itself.

Finally, institutional care places vulnerable individuals in close, frequent contact, which promotes transmission of microorganisms. This contributes to the high risk of outbreaks of infection in long term care facilities.

Unique aspects of Long Term Care Facilities

The long term care facility is a low technology environment which is a permanent home for many residents (2). The principle goal of management is not to “cure”, but to maintain as high a quality of life as possible, given the substantial comorbidities and impaired functional status of residents.

Management of infections in long term care facilities is frequently problematic because of diagnostic imprecision (3). Evaluation of new or changed signs and symptoms is often impaired by difficulties in communication and the presence of chronic symptoms. Access to laboratory and radiologic diagnostic testing may be limited, and results of testing delayed. The interpretation of positive bacterial cultures is compromised by the high prevalence of bacteriuria or oropharyngeal and wound colonization with potential pathogens (1).

This diagnostic imprecision contributes to the problem of excessive and inappropriate antimicrobial use in these facilities, promoting antimicrobial resistance as well as causing adverse effects in individual patients (4). One approach to addressing antimicrobial use has been the development of consensus guidelines which define clinical presentations where initiation of empiric antimicrobial treatment is appropriate (3). For instance, for urinary tract infection in the resident without a chronic indwelling catheter, antimicrobials should not be initiated unless there is acute dysuria, by itself, or one of fever, increased confusion, or rigors with at least one localizing genitourinary symptom - urgency, frequency, suprapubic pain, gross hematuria, costovertebral angle tenderness or new or increased urinary incontinence. These guidelines have been evaluated in a prospective randomized study and shown to be safe and, at least for urinary infection, decrease the inappropriate use of antimicrobials.

Prevention of Infection

Most of the factors which contribute to infection in the elderly are not amenable to alteration. However, both individual patient measures and infection control programs may prevent some infections (2, 5). Patient care should include optimal management of co-morbidities, maintaining functional status, avoiding invasive devices if possible, skin care programs, and appropriate vaccinations. Guidelines for infection control programs for long term care facilities have been developed (2). Infection control programs may, however, be compromised relative to acute care facilities because of characteristics intrinsic to the long term care facility such as resource limitations, limited staff expertise, high staff turnover, or limited access to diagnostic facilities. The relative effectiveness of discrete infection control program components have not been evaluated in clinical trials. However, effective interventions likely include outbreak prevention and control, influenza vaccination of residents and staff, appropriate environmental management including food practices and cleaning of shared equipment, and restriction of ill workers.

Resistant organisms are usually initially acquired in an acute care facility, and infection in the long term care facility resident is relatively infrequent given the high prevalence in some long term care facilities (2, 5). However, colonized residents usually have prolonged carriage. Assiduous compliance with hand hygiene, appropriate environmental cleaning, and optimal antimicrobial use are recommended for managing resistant organisms in long term care facilities (2). Additional precautions such as isolation or cohorting, activity restriction, barrier precautions, and screening are controversial and have not yet been adequately evaluated to determine whether they are beneficial. Restrictive interventions which may have a negative impact on

quality of life should be introduced only with evidence that colonized individuals are a risk to themselves or others in the facility, and not simply because of the presence of colonization.

Conclusion

The ultimate goals of care for residents of long term care facilities is to maintain quality of life, ensure safety of the resident, and to achieve this in a cost-effective manner. Infections which occur in residents of long term care facilities may impair all of these and, thus, are an important problem. Long term care facilities need to ensure optimal medical care of patients, as well as maintaining appropriate and effective infection control practices to limit, wherever possible, the acquisition and transmission of infection.

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SURVEILLANCE AND MANAGEMENT OF INFECTIONS IN LONG TERM CARE FACILITIES OF LOMBARDY REGION

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Introduction

By 2030, the population >65 years old will double and >85 years old will triple. More than 40% of the elderly will spend at least some time in a Long Term Care Facility (LTCF) due to functional limitations that will make them unable to manage independently in the community.

The aging population of Italy represents an increasing public health priority: citizens living to “old-old” age, i.e. older than 85 years, comprise the most rapidly growing group in society.

In Lombardy (10 million inhabitants) the trend of smaller families and the dispersion of family members leads to increase long-term care services and the percentage of over 65 population/total resident population will rapidly increase. LTCFs are located and distributed in all regional district areas with different characteristics in order to provide for all patients' needs in a very heterogeneous population.

LTCFs in the Region include 54,581 beds in residential institutions for providing nursing care, 7,830 beds in hospital and 3,121 in non-hospital settings devoted to providing rehabilitation care (neuromotorial, cardiovascular, respiratory).

The risk of infection in these facilities is increasing for a number of reasons: a greater circulation of multi-drug resistant organisms (MDROs), reservoirs of resistance, patients transferred from the acute care to the LTCF settings, structural factors related to the facilities, low-technology, understaffing and overcrowding.

On June 21, 2007, the General Directorate of Health in Lombardy established a Working Group on Infections in Rehabilitation Units to increase knowledge of the burden of infections and to face and solve the related emerging problems in these facilities. Overall objectives include monitoring, increased knowledge, surveying, measurement, control, prevention, efficacy; some possible strategies were identified to describe the epidemiology of nosocomial infections, including trends and microbiological aspects.

Materials and methods

Data have been extracted from the Central Database of Lombardy Department of Health and from hospital databases participating in the study between 2005-2006.

The eligibility criteria for the epidemiological analysis included the ICD-9-CM

hospital discharges diagnosis codes (ICDDC) belonging to the following ten main infectious diseases grouping: UTIs (urinary tract infections), low respiratory tract infections, intestinal infections, sepsis, candidiasis, not specified bacterial infections, skin and soft tissue infections, iatrogenic infections, cardiovascular infections, bone infections. The validation of ICD-9-CM diagnosis was performed by direct medical charts review, in order to assess and maximize the validity of the method. 123 hospital rehabilitation units with 7,830 beds were considered in the study; ICD-9-CM medical charts corresponding to 184,916 hospitalizations, 149,471 patients and 14,201 ascertained cases were included in the analysis; 3,246 medical charts were validated in 33 of the 123 hospital rehabilitation units. Logistic regression was performed in the statistical analysis.

A workshop and two audit sessions (to better understand processes currently employed in rehabilitations and microbiological units and relative needs) were organized in 2007 and 2008. 23 Rehabilitations Units and 19 Laboratories of Microbiology participated in the Questionnaire Audit Sessions (QAS) mainly related to the management of indwelling catheters, relative UTIs and about local microbiological flora in these facilities.

Results

Results show a distribution by age of the cohort gradually increasing from the lower to the higher ages and a longer stay (mean) from 9 to 13 days in patients with infections and in particular in hospitalized females and in neurorehabilitation units. With respect to age, we estimated excess risk of any nosocomial infection ranging from 38% (45-54 years) to 426% (more than 85 years), compared to age <45 years. The incidence x 1000 was evaluated in geriatric rehabilitation (general), cardiorespiratory and neurological wards, with estimates of 220.7, 70.3 and 74.4 respectively. The risk per place of origin (hospital vs. community) was also considered, with incidence resulting in 91,6‰ and 57,9‰, respectively.

Potential cases of UTIs are markedly prevalent (38‰), followed by low respiratory tract infections, overall bacterial, skin and soft tissue infections, sepsis, candidosis, iatrogenic, cardiovascular, bone, intestinal with estimates at 13,7‰, 14,0‰, 13,4‰, 2,50‰, 0,60‰, 8,99‰, 1,80‰, 0,50‰, 2,20‰ respectively.

Preliminary results obtained from medical charts validation analysis show an underestimation in ICD-9-CM hospital discharges diagnosis of infections: 306 unreported diagnosis (SDO) among 2,124 medical charts submitted to a preliminary validation analysis. It seems that the infection rate is higher than one estimated based only on ICD-9-CM hospital discharges diagnoses. The microbiological results, related to years 2005 and 2006 in 12 Rehabilitation Units, show a total number of positive culture for microorganisms of 13,771 and 13,705 and a rate of positive urine cultures for ESBL of 7,05% and 7,66% respectively.

The answers obtained from urinary catheter management audit sessions related to screening, evaluating appropriateness and use, care planning, monitoring use, reevaluating use, policy assessment, staff education and training, reveal that some topics need improvement. In particular some of the 27 given answers are not in accordance with the current procedures of catheter management: the large

heterogeneity in protocols, the antibiotic treatment employed in bacteriuria, the unremoved catheter before starting antibiotic, the low number of hand washing among the staff before and after catheter insertion and the lack of consulting ID specialist in case of antibiotic treatment .

Three different phases of UTIs microbiological management (pre, analytical and post) were evaluated during a specific audit session by 16 questions about different topics to 19 Medical Directors of Microbiology Laboratories. Answers show in three topics only a slight lack of adherence to current procedures: namely urine culture request informations, reported time of urine specimen collection and the indication of bacterial load per single specimen.

Discussion

The ICD-9-CM discharge diagnosis codes are useful in a large scale regional network of LTCFs (Rehabilitations Units/Nursing Homes) to enhance the ability of monitoring the epidemiology, the outcome definition, the comorbidity profiles, drug consumption, infection-related sentinel events.

The ICD-9-CM medical charts validation is required to maximize the validity of the method and to reduce the bias particularly due to underestimation. Preliminary results confirm the importance of the validation analysis and the underestimation of infection rate in the different considered infection areas.

Audit Session methodology is very important to involve directly medical and non-medical staff members in order to assess and to improve the management and clinical processes employed in LTCFs. Additional time should be required in this methodology to co-ordinating further activities.

Infection control strategies in UTIs (expecially concerning chronic indwelling catheters management) are priorities to develop by a case/control study to organize in Lombardy LTCFs.

The epidemiological monitoring of microbiological data, the molecular mapping of MDROs (e.g.ESBL, MBL, MRSA, Acynetobacter, VRE), C. difficile and the record linkage with ICD-9-CM discharge diagnosis codes medical charts are very important steps to completing the infection control strategies in the LTCFs.

A regional network infections surveillance database, devoted to LTCFs, could be helpful in for the prevention and control of infections.

HEALTHCARE ACQUIRED INFECTIONS IN THE ELDERLY: SURVEILLANCE AND CONTROL ACTIVITIES IN THE EMILIA-ROMAGNA REGION

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In the last decade, the problem of healthcare acquired infections in residential facilities for the elderly has been increasingly considered a critical public health issue: several papers have documented the high prevalence of infection in this setting in Europe (1, 2) and an increasing trend of antimicrobial resistance has been reported (3).

At the same time, some authors have documented the efficacy of infections control prevention in nursing homes, and specific guidelines have been issued (4), even though some authors have emphasized the scarcity of experimental studies on infection control measures in long-term care: a recent example is MRSA control in nursing homes for older people (5).

To evaluate the feasibility of basic measures to control infection transmission in nursing homes, an intervention program has been conducted in the Emilia-Romagna region.

Materials and methods

The study was carried out in 19 residential facilities of three Local Health Authorities (LHA) of the Emilia-Romagna region: 11 facilities in 2 Health Authorities targeted infection control prevention, while eight targeted pressure ulcers.

The intervention consisted of the followings:

- a task force was created in each LHA, with the aim of reviewing the practices adopted and identifying the need for change;
- a survey to describe knowledge and perceived practices of health and social care workers was carried out, to identify critical issues;
- an educational programme was conducted;
- “good clinical practices” were agreed and needed resources/structural changes identified.

The intervention, in the 11 facilities which have decided to targeted infection prevention, has been evaluated using both outcome and process measures:

- a) the frequency of infection, detected by means of six point-prevalence surveys and, in selected facilities, by continuous surveillance;
- b) the achievement of targeted actions (protocols and operative procedures related to infection-control practices), after the intervention.

Results

The 11 participating facilities were owned in 8 cases by public institutions, in 1 by private for-profit, and in 2 cases by private non-profit organizations. Overall, the facilities accounted for 760 beds, and about 500 healthcare and social workers.

The Knowledge and Practice Survey, conducted before the intervention was started,

TABLE 1 - *Actions included in the intervention program to control infections.*

<i>General action</i>	<i>Specific activities</i>
Improve hand hygiene and glove use	Written protocol for hand hygiene and glove use Survey of available resources for hand hygiene Introduction of alcohol-based products for hand hygiene Tailored strategy to reinforce good practice over time
Improve basic hygienic care	Written protocol for basic care of the elderly Implement audit activities for elderly basic care Soap dispensers, paper towels, and waste baskets in each elderly bathroom
Improve the antiseptics, disinfection and sterilization practices	Written protocol for antiseptics/disinfection/sterilization practices Written procedure for autoclaves maintenance Supply of necessary decontamination products/ instruments Procedure for LHA central sterilization (for facilities lacking sterilization machines)
Improve the management of residents with urinary catheter, PEG or respiratory therapy	Written protocol for residents with urinary catheters, PEG, or respiratory therapy and interventions to promote good practice
Improve the timely diagnosis of infections	Written protocol for timely diagnosing infections Form for recording signs and symptoms of infections daily and implementation through an educational program Standardized procedure for assuring the timely access to appropriate diagnostic testing Written protocol for appropriate antimicrobial use and monitoring of prescriptions
Increase the vaccination coverage (flu for health care workers-HCWs; flu and pneumococcal infections for residents)	Reviewed vaccination policy Tailored strategy to reinforce HCWs vaccination coverage
Improve training of HCWs at arrival in the facility and over time	Biannual educational plan for all HCWs

allowed to identify several areas which needed to be improved: among the 16 respondent physicians, less than 50% correctly identified recommended practices for controlling epidemics of specific infections, were aware of the indication of not prescribing antimicrobials in asymptomatic bacteriuria, knew basic pharmacodynamic parameters related to antimicrobials. Among the 58 respondent nurses, the most critical issues identified were those related to basic hygienic measures (oral care, diabetic foot care, etc.), knowledge of basic principles related to sterilization and disinfection, and of selected recommended practices for invasive procedures. Similar critical issues emerged for the 323 respondent health and social care workers. To improve care practices in participating facilities, the actions reported in Table 1 were planned.

Infection prevalence was highly variable by individual facilities and over time; a

clear trend was not identified. In one facility the comparison of prevalence data with continuous surveillance demonstrated that prevalence surveys are not sufficiently accurate to detect infection variation attributable to possible infection clusters.

Monitoring of targeted actions over time showed that:

- 1) all participating facilities implemented written protocols for the defined items, except for appropriate antimicrobials prescribing;
- 2) the necessary resources were assured in all facilities;
- 3) the vaccination policies have been improved;
- 4) the least satisfactory actions were those related to continuous infection surveillance, health personnel information and training, and intervention aimed at assuring sustained improvement over time.

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NEW MODELS FOR ANTIBIOTIC TREATMENT OF INFECTIONS CAUSED BY HIGHLY DRUG-RESISTANT BACTERIA

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Antibiotics have been used to treat bacterial infections for over 60 years. Early after their introduction, bacteria began to express resistance to these drugs and this spawned an entire new science related to the mechanisms bacteria developed to resist the action of antibiotic “wonder drugs.” Over the past six decades many “classes” of antibiotics have been introduced, more or less keeping pace with the incursion of antibiotic-resistant bacteria. However, the current situation has shifted in the direction of the resistant bacteria and today the balance is leaning in their favor!

While most serious bacterial infections can be treated, physicians most certainly will face continued challenges as a result of world wide increases in the prevalence of antibiotic resistant bacteria.

The major antibiotic-resistant infecting organisms include vancomycin-resistant *Enterococcus faecium*, *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae*, *Acinetobacter baumannii*, fluoroquinolone-resistant *Pseudomonas aeruginosa* and *Enterobacter* species (1). Bacteria have “learned” how to resist the action of almost all antibiotic classes and the development and production of new antibiotics to treat resistant organisms have not kept pace with the bacteria.

Currently a gap exists between the “bad bugs” and “new drugs” so that physicians might soon face the inability to treat larger numbers of patients infected with resistant bacteria, and to some extent we risk returning to the pre-antibiotic era if new solutions are not found soon. An IDSA task force has recently reviewed the current and expected antibacterial pipeline (1).

In the absence of new antibiotics it is imperative to develop new paradigms or “models” to maximize the current therapeutic armamentarium and minimize the further development of antibiotic resistant pathogens.

Some obvious approaches include the use of selected older and potentially toxic antibiotics such as colistin, unique antibiotic combinations such as gemifloxacin plus cotrimoxazole for MRSA or linezolid plus doxycycline for *E faecium* (2), optimizing antibiotic stewardship, antibiotic rotation schemes, limiting the duration of antibiotic therapy and prophylactic use, etc. Data from experimental animal studies and those from novel *in vitro* dynamic models have supported the application of pharmacokinetic and pharmacodynamic (PK/PD) principles to maximize the antimicrobial effect and, more recently, to minimize the selection of antibiotic-resistant bacteria. Several parameters have been shown to predict antibiotic effects in *in vitro* and *in vivo* models.

For example, concentration-dependent antimicrobial effects of fluoroquinolones and aminoglycosides are better predicted by AUC/MIC and C_{\max}/MIC , whereas

time-dependent effects of penicillins and cephalosporins are better predicted by time above the MIC (3). *In vitro* models have been particularly useful in these pre-clinical studies and have validated or replicated findings from experimental animal studies. Several investigators have reported the ability of applied PK/PD principles to optimize the antimicrobial effect and minimize bacterial resistance (4-7). Drlica and Zhao defined the concept of the mutant prevention concentration (MPC), the lowest concentration of drug that will prevent mutant enrichment *in vitro* and the mutant selection window (MSW), that concentration between the MIC and the MPC (8). This concept was validated in our *in vitro* studies with fluoroquinolones (9), daptomycin and vancomycin (10).

Moreover, bell-shaped relationships were established for AUC/MIC and the selection of resistant *S. aureus* (9, 10) and *S. pneumoniae* (4). Recent data suggest that the ratio of AUC to MPC might be a powerful predictor of activity against resistant mutants and might inform the dosing of antimicrobial drugs to prevent selecting bacterial resistance during therapy.

In one study from our laboratory, the AUC_{24}/MPC of ciprofloxacin was more predictive of the selection of resistant mutant staphylococci than was the AUC_{24}/MIC (11).

In another *in vitro* model study the addition of low exposures of doxycycline prevented the selection of resistant *E. faecium* during simulated linezolid treatment (2).

Pre-clinical studies in animals and using *in vitro* dynamic models can inform??? the dosing of antimicrobials to maximize their effect and minimize the selection of resistant bacteria. Some of these concepts have been validated in clinical studies but further investigation is needed.

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ANTIFUNGAL TREATMENT AND DIAGNOSTIC TESTS OF NEW GENERATION

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The management of fungal infections has greatly improved in recent years, with the advent of new drugs very active against both *Candida* and *Aspergillus*. These include drugs belonging to the triazole and echinocandin families. In addition, lipid amphotericin B compounds remain widely used, because of their very large spectrum of activity and improved tolerability. In aspergillosis, clinical trials have shown response rates as high as 50%, although efficacy in proven/probable infections is lower (probably between 35% and 45%) and is strongly influenced by the status of the underlying disease.

The 2 drugs recommended for first line therapy by most if not all national and international guidelines are voriconazole and liposomal-AmB (L-AmB). Good results in prophylaxis have been achieved by posaconazole, despite an erratic absorption. In invasive candidiasis response rates as high as 70%-80% have been obtained by many drugs (echinocandins, L-AmB, voriconazole). The American guidelines recommend an echinocandin or, in stable patients, fluconazole, while European guidelines include voriconazole as well. However, a more careful look at the results of clinical trials show that patients with deep-seated infections have much lower response rates, in the range of 25-30%.

Overall mortality remains high (around 40%). When considering that in clinical trials patients are included according to predefined inclusion and exclusion criteria, which usually exclude very sick patients, it is likely that the situation in terms of mortality might be not so optimistic, both in aspergillosis and in candidiasis. There is a general trend in many, but not all, hospitals to abandon empirical antifungal therapies, and to use a more watchful therapeutic approach. This is mainly due to the availability of new diagnostic tools.

The detection of galactomannan in serum and other body fluids, accompanied by imaging studies and clinical evaluation has become essential for managing leukemic patients and recipients of allogeneic transplantation. The usefulness of the beta-D-glucan test in these patients is still partially investigational, especially because of its lower specificity. Provisional data coming from several authors (including ourselves) seem to show that this test might be useful in intensive care units (ICU), as well. Clinical prediction rules have also been suggested, that are apparently able to identify patients at high risk of invasive candidiasis in ICU. Combining the prediction algorithms with the laboratory tests seem a logical conclusion to drive early therapy and avoid overtreatments.

MOLECULAR CHARACTERIZATION OF STRAINS OF CLOSTRIDIUM DIFFICILE ISOLATED FROM HOSPITALIZED GERIATRIC PATIENTS

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Introduction: *Clostridium difficile* (Cd) is a spore-forming, gram positive anaerobic bacillus. It can be found as commensal in the human intestinal flora. Cd is the etiologic agent of pseudomembranous colitis and the most common cause of nosocomial antibiotic-associated diarrhea. The pathogenic strains produce toxins (A and B) with cytotoxic effects on intestinal epithelium. Some strains producing binary toxin, cause more severe infections. So far it is not known the specific role of this toxin.

The major risk factors for acquiring this infection are: advanced age (over 65), underlying disease, severity of illness, antibiotic exposure and prolonged hospitalization. The purpose of our work was to perform a molecular characterization of Cd strains isolated from patients hospitalized at ASP Pio Albergo Trivulzio. We also performed the analysis of sequential isolates in order to verify if the recurrent infections were due to relapse or reinfection.

Methods: A total of 100 C.d. isolates were collected from 75 symptomatic patients from 6 different hospital wards. The strains were cultured on blood agar plates (CD agar - bioMérieux) in an anaerobic atmosphere for 48 h at 37°C. The identification of species was performed using Vitek automated system (bioMérieux). The molecular typing was performed by “ribotyping” according to the method described by Bidet et al., using the 16 S (5'-GTGCGGCTGGATCACCTCCT-3') and 23 S (5'-CCCTGCACCCTTAATAACTTGACC-3') sequences. Furthermore, all strains were subjected to PCR to detect the presence of the gene coding for binary toxin.

Results: The analysis of patterns obtained by ribotyping showed 14 different ribotypes. None of the strains tested was found to produce binary toxin.

Conclusions: The data obtained indicate that there is a considerable spread between the same ward in respect of the spread between different wards. For this phenomena we can assume that the spread has been fostered by the movements of patients in different rooms and that the environment is a possible source of infection. Most of the sequential samples belong to the same ribotype indicating that the recurrent infections may be due to relapse from treatment failure or reinfection with the same strain. The lack of toxin-producing strains binary allows for the time being, not to further increase the rate of mortality.

PHENOTYPIC AND GENOTYPIC CHARACTERIZATION OF INVASIVE *STAPHYLOCOCCUS AUREUS* ISOLATES IN ITALY

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Objectives: As methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the leading causes of morbidity and mortality in hospital settings we examined nosocomial invasive *S. aureus* strains in order to characterize them both microbiologically and epidemiologically by phenotypic and genotypic methods.

Methods: In the period 1 September 2006 - 28 February 2007, 147 invasive *Staphylococcus aureus* strains were obtained from 19 hospital laboratories distributed all over the country. Susceptibility to antibiotics were assayed by automated systems; MICs to glycopeptides were confirmed by E-Test. CLSI breakpoints were applied. The *agr* group and the SCCmec were determined by PCR. The repeat region of the *S. aureus* protein A (*spa*) gene was sequenced and analysed by the Ridom Staph Type software. MLST was also performed.

Results: Out of 147 isolates, 81 were MSSA and 66 MRSA. By automated system all the isolates were susceptible to vancomycin, teicoplanin and linezolid. Resistance to ciprofloxacin, erythromycin, gentamicin, clindamycin and rifampin was found in 45%, 38%, 33%, 33% and 9% of the isolates, respectively. 4% of isolates was found resistant to tetracyclin; By E-Test vancomycin susceptibility for MSSA was: MIC₅₀ = MIC₉₀ = 1.5 mg/L; for MRSA: MIC₅₀ = 1.5 mg/L, MIC₉₀ = 2 mg/L. Only among MRSA, 3 strains were VISA (MIC = 3 mg/L). By *spa* typing, MSSA were highly heterogeneous. Among MRSA three main groups were identified: t041(23 isolates), t008(19 isolates) and t001(9 isolates). Out of 3 VISA, 2 were assigned to *spa* type 041. All the isolates assigned to *spa* type 041 harboured SCCmec type I and *agr* 2. By MLST, selected strains among those characterized by *spa* type 041, including one VISA strain, belonged to clonal complex (CC)5.

Conclusions: Most invasive *S. aureus* Italian isolates showed reduced susceptibility to vancomycin. Among MRSA, 3 VISA strains emerged and *spa* type t041 was the most frequent nosocomial *spa* type.

INCREASING OCCURRENCE OF PLASMID-MEDIATED AMPC BETA-LACTAMASE PRODUCING PROTEUS MIRABILIS CAUSING BLOODSTREAM INFECTIONS

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Background: Plasmid-mediated AmpC beta-lactamases (CBLs) have been increasingly reported over the last few years. However, prevalence and distribution of CBLs among enterobacteria are still largely unknown. The aim of this study was to evaluate the CBL production in blood culture isolates in comparison with the production of extended-spectrum beta-lactamases (ESBLs).

Methods: Enterobacteria obtained from blood cultures performed at the Manzoni Hospital (Lecco, Italy) during a 5-year period (2004 to 2008) were included in the study. Identification and antimicrobial susceptibility were carried out using the VITEK 2 instrument (bioMérieux). ESBL and/or CBL production were assessed according to CLSI criteria (when available) and confirmed by molecular methods.

Results: Overall, 45 ESBL-positive isolates were detected, including *Escherichia coli* (n=29), *Proteus mirabilis* (n=5), *Klebsiella pneumoniae* (n=5), *Enterobacter cloacae* (n=2), *Enterobacter aerogenes* (n=2), and *Serratia marcescens* (n=2). No significant differences were observed over the years (2004, n=5; 2005, n=10; 2006, n=11; 2007, n=11; 2008, n=8). On the contrary, CBL production was detected solely in *P. mirabilis* isolates (n=6), starting from February 2007 from a neurosurgical patient. The remaining 5 isolates were collected from February to August 2008 from patients admitted to different wards. Carbapenems (ertapenem, imipenem, and meropenem) and amikacin were consistently active against both ESBL- and CBL-positive isolates.

Conclusions: *P. mirabilis* isolates producing CBLs have emerged among enterobacteria causing bloodstream infections in our hospital. Together with ESBL-producing enterobacteria, they represent a new challenge for physicians and microbiologists. Carbapenems and amikacin show potent *in vitro* activity against both ESBL- and CBL-positive isolates thus representing a valid therapeutic option for treating infections caused by these MDR pathogens.

FIRST REPORT ON *K. PNEUMONIAE* STRAINS PRODUCING BOTH VIM AND CTX-M TRANSFERABLE ENZYMES

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Objectives: The recently reported emergence of carbapenem resistance among metallo- β -lactamases (MBLs)-producing *Enterobacteriaceae* is a matter of clinical concern.

The aim of this study was to screen for the presence of beta-lactamases among *Klebsiella pneumoniae* clinical isolates showing reduced susceptibility to carbapenems.

Methods: During the period 2007-2008, 30 *K. pneumoniae* isolates with reduced susceptibility to carbapenems were collected from a Rehabilitation Facility located in Pavia, and two acute care hospitals, one placed in the same city and the other in S. Giovanni Rotondo. MBL and Extended-Spectrum β -lactamases (ESBLs) production were screened by the use of IPM-EDTA and double disc synergy tests, respectively. Imipenem (IPM) MICs were determined by both E-test and broth macrodilution methods (CLSI 2008).

Isoelectric focusing (IEF) was performed with crude cell extracts of all the potential ES β L producers. The β -lactamase genes were identified by PCR and sequencing. Genomic DNA, digested with XbaI, was subjected to PFGE. MBL and ESBL genes transferability was investigated by conjugation and plasmids were characterized by RFLP analysis.

Results: The IPM-EDTA disc synergy test yielded a positive result in 14/30 strains, characterized by IPM MICs ranging from 2 to 128 mg/L. PCR experiments detected *bla*_{VIM-1} like genes in the same 14/30 isolates. The sequenced *bla*_{VIM-1} gene was located on a conjugative plasmid; *bla*_{SHV-5} and *bla*_{CTX-M-1} genes resulted co-transferred in 11/14 and 3/14 cases respectively.

VIM-1 producers were revealed in all hospitals. Two clones were detected, both responsible for outbreaks. The clonally related *K. pneumoniae* isolates collected from 6 different wards of the Pavia acute hospital harboured different conjugative plasmids 80-90 kb large; an identical conjugative plasmid 85 kb large was while characteristic of the strains from the S. Giovanni Rotondo hospital ICU.

Conclusions: This is the first report on the emergence of a MDR clone of *K. pneumoniae* producing VIM and CTX-M transferable enzymes.

Control measures including screening by IPM-EDTA synergy tests should be routinely applied to detect MBL producing strains and to contrast the vertical and plasmidic diffusion of carbapenem-resistant *K. pneumoniae* in acute care and rehabilitation facilities.

INFECTION SURVEILLANCE IN RSA (NURSING HOME) PATIENTS

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Elderly patients are exposed to infections, due to their anatomical, physiological and functional characteristics, especially when institutionalized or in hospitals. Well-known risk factors for nosocomial infections are comorbidity, functional and cognitive impairment, pressure ulcers, invasive devices.

These are common features in RSA (nursing homes) residents, so that one can expect to find some occurrence of infections. The RSA at Istituto P.Reddaelli in Milano (about 300 beds) contains most of all very old patients (average age 83), dependent in basic ADL, with elevated medical complexity, often cognitively impaired. Besides, inside this RSA there are a 40 beds ward for patients with severe cognitive impairment and behavioural disturbances (NARSA) and a 12 beds unit for patients in vegetative state (SVP). In order to test the stated hypothesis we performed a longitudinal study on 3 units: one RSA unit with 46 beds (3PR), an Alzheimer ward (NARSA) and the SVP unit. The study lasted 1 year (from Jan.1st to Dec.31st 2008). To detect diagnosis of infections we used the Mc Geer criteria for infection surveillance in long term care facilities. The criteria have been modified for SVP patients, since they are not able to explain subjective symptoms.

The results of the identifications of pathogens in all the samples sent to the microbiology lab of the Istituto by the 3 units all the year long, have been recorded. The incidence in 3PR was 45 events in 16481 patient-care days (2,73/1000 days); in NARSA it was 53 events in 14997 days (3,53/1000); in SVP 39 episodes in 3329 days (11,72/1000). It is important to stress that in all 3 areas more than 50% of the events consisted of lower respiratory infections: 65% in 3PR, 53% in NARSA, 58% in SVP. As a second more frequent infection in NARSA and 3PR, skin/soft tissues/wound (CTF) infections, respectively 26% and 16%. Only in SVP the second infection was UTI (28%) and the third was CTF with 10%. 46 strains of pathogens were isolated in 3PR, 20 in NARSA and 128 in SVP. In 3PR 63% of the isolates were enterobacteriaceae (basically *E.coli* and *Proteus mirabilis*); nearly the same in NARSA (65%); in SVP Enterobacteriaceae were 41%, *Pseudomonas aeruginosa* 14%. The most relevant results in spectrum of resistance of the isolates show a strong presence of ESBL+ in SVP (100% of *E. coli* and 90% of *Proteus mirabilis*). The evidence of carbapenem-resistant *Pseudomonas aeruginosa* in SVP (28%) is particularly interesting.

In conclusion, infections in nursing homes are a relevant aspect, particularly amongst patients at higher risk, so that it becomes one of the major clinical problems in SVP patients. Also the occurrence of multi resistant pathogens, representing a typical hospital flora, is related to a higher risk.

AUDIT ON HIGH COST ANTIBIOTICS USE IN A DEPARTMENT OF INTERNAL MEDICINE: A PRELIMINARY REPORT

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Background: Increasing rates of resistance to antimicrobials among hospital pathogens is a worldwide problem that has been recognized for more than twenty years. The consequences of resistance are well known, including increased morbidity, mortality and costs of healthcare.

Inappropriate antibiotic use is recorded in 25-50% of hospital prescriptions. Antibiotic misuse is common in empirical and targeted therapy. The major reasons for inadequate therapy are the use of antibiotics with unnecessarily broad spectrum and longer than needed duration of therapy. Many clinicians have a limited perception of the problem of antimicrobial misuse and resistance therefore multiple strategies have been developed to optimize the therapeutic management. In our Department of Internal Medicine during the 2007 the cost DDD of antibiotics was 4,86 respect to 4,13 of the previous years.

Objective: To evaluate the appropriateness of high cost antibiotics use in a large department of internal medicine of an University Hospital of North Italy.

Methods: A retrospective audit was performed between may and december 2008 to analyze antibiotics treatments with piperacillin - tazobactam, meropenem, teicoplanin and linezolid in hospitalized patients in the 2007. The study was carried out by reviewing all medical records of patients who received one or more of the antibiotics about reported. The appropriateness of the treatments was studied with regard to the bacteriological results, serious infections, risk factors, multiple morbidity and previous failures.

Results: 146 high cost antibiotic prescriptions of 110 patients were analyzed during the study period. 81,5% of prescriptions were appropriate with regard to the criteria used. Piperacillin/Tazobactam and Meropenem were used often as etiologic therapy. The rate of inappropriate teicoplanin use was of 28,8%.

Conclusions: This audit conducted in a department of internal medicine reveals that the appropriateness of high cost antibiotics prescriptions was significantly higher if compared with other as surgical wards. Antibiotics against gram negative were adequate. An important rate of inappropriate high cost antibiotic prescriptions was observed for teicoplanin, confirming the need to develop control strategies regarding the utilization of antibiotics in order to control the diffusion of multiresistant bacteria. The informations obtained of our audit may improve the appropriateness of antimicrobial therapy in the internal ward with reduction of the mortality.

EFFECT OF CMV-IMMUNOGLOBULINS (CYTOTECT BIOTEST) PROPHYLAXIS ON CMV PNEUMONIA AFTER LUNG TRANSPLANTATION

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Introduction: Lung transplant (LT) recipients among solid organ transplant recipients are at high risk for cytomegalovirus (CMV) infections. The clinical symptoms related to CMV disease and the prevention of CMV infection show variation among different patient populations, depending on the type of transplant and the intensity of immunosuppression. The two main approaches for prevention of CMV disease are prophylaxis and preemptive therapy with currently available antiviral compounds. We evaluated the effect of CMV-Immunoglobulins (CMV-IG) (Cytotect Biotest) on CMV pneumonia diagnosed in 303 follow-up transbronchial biopsies (TBB) of lung transplant recipients.

Methods: At our Centre 24 patients (control group, 155 TBB from 1999 to 2002) received acyclovir for 24 months and 33 recipients (study group, 148 TBB from 2003 to 2008) received a combined CMV prophylaxis consisting of CMV-IG (Cytotect Biotest) at day 1,4,8,15,30 and monthly for 12 months and a short Ganciclovir or Valganciclovir therapy from 21th postoperative day for 3 weeks followed by acyclovir up to 24 months. Statistical analysis was performed using Chi-square test for proportion differences.

Results: In our study the percentage of pneumonia at first month TBB was similar in study group vs control group, 9.1% (3/33) vs 8.3% (2/24), p=0.9 ns, but after the first month the percentage was significantly lower in study group in first year at follow-up TBB (months 3,6,9,12), 1% (1/99) vs 6.4% (5/78), p=0.048, and in first two years follow-up TBB (months 3,6,9,12,18,24), 0.8% (1/122) vs 6.5% (8/124), p=0.018.

Conclusions: Our data suggest a strong efficacy of CMV-IG prophylaxis in reducing CMV pneumonia after first month in lung transplant recipients. The effect of first year post transplant combined prophylaxis seems to be useful in preventing not only first year but also second year CMV pneumonia suggesting some long lasting immunological role of prophylaxis that needs more studies to be better defined.

SIMPLE CRITERIA SUGGESTIVE FOR PULMONARY TB

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Tuberculosis represents a major problem developing countries.

Diagnosis is often difficult and often relay on clinical criteria and simple laboratory examinations, as cultural methods and molecular biology are not available in most health facilities.

Data from patients from Wolisso Hospital, rural Ethiopia, are presented.

117 patients were examined in the period from April 2006 to September 2008 and diagnosis of TB was made, by sputum examination, or by typical chest X-ray.

Sex distribution was 52 males and 75 females, mean age 31 years (range 10-75).

Patients' history showed cough for more than 99%, for an average of 3,2 months (1 week to 2 ears), 96.6% of which was productive; sputum was mucoid in 55%, and bloody or purulent in 22% each, weight loss was complained by 87%, a previous contact with TB patients was reported by 25%, sharp chest pain was present in 81%, sweating in 88%, weakness in 95%, fever in 84%, dyspnea in 77%, HIV rapid test was performed in 32 patients, resulting positive in 5 (15.6%)

Clinical data show low mean BMI (16.2, 10-23), low BP values (mean sys BP 99 mm/Hg, 70-180; mean dia BP 64 mm/Hg, 40-110), tachycardia (mean HR 104 bpm, 64-150). Standard laboratory examinations showed significant ESR increase (mean 69, 4-148), normal mean WBC count (7.2 cells/mm³, 2.6-13.5) and neutrophil predominance in all samples, normocytic anaemia (mean Hb 9.5 g/dl, 4.4-14.8; mean MCV 83) and normal mean platelets count (313x10³, 145-508).

In conclusion patients who previously lived in developing countries can be considered at high risk of pulmonary TB in case of long lasting cough (>1 month), dyspnea, chest pain, weight loss, fever weakness and night sweats; typical physical examination emaciated condition, with low BP and BMI; simple laboratory examinations suggestive for TB are high ESR and normocytic anaemia. Absence of known TB contact and bloody sputum are not significant to rule out TB, and WBC total and differential count are not useful for the diagnosis.

THE FRENCH NATIONAL INFECTION CONTROL PROGRAM: DEVELOPMENTS AND ACHIEVEMENTS

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The French program for prevention and control of health-care associated infections (HAI) were initiated in France in 1988 by the creation of an infection control committees in each hospital. However, it was not until 1992 that a national organization was set up, with the appointment of an advisory expert committee to advise the MoH on priorities and actions. A comprehensive national program has gradually been set up in France over the period 1993 to 2004, which included strengthening of organization for infection control activities at the local, regional and national levels, and development of large networks for surveillance of specific infections and control of antibiotic resistance; the organization was complemented in 2001 by the mandatory notification of unusual nosocomial events, notably of outbreaks to allow early detection and rapid response to sentinel events.

The organization for surveillance and control of HAI developed in France has been progressively strengthened from 1992 to 2004 to include infection control structures at the local and regional levels, which are coordinated by 5 inter-regional coordinating centres and national structures, and a comprehensive surveillance and alert system based on:

- 1) National prevalence studies, performed every 5 years since 1996;
- 2) networks for surveillance of the incidence of priority infections and events, which are based on voluntary participation of hospitals and use a common methodology; these include a network for multidrug-resistant bacteria (MDRB), blood and body fluid exposures (BBFE) of personnel, nosocomial bacteraemia, and infections in ICUs. Each of the 5 inter-regional centres coordinate one of these national network, but all networks have been gathered since 2001 within a network of networks (the RAISIN, <http://www.invs.sante.fr/raisin/>) under the coordination of the National Institute for Public Health Surveillance (NIPHS);
- 3) detection of sentinel events through mandatory notification to the health authorities, inter-regional coordinating centres and NIPHS;

Building on these structures, the program 2005-2008 set up new goals and objectives http://www.sante.gouv.fr/hm/dossiers/nosoco/copil_programme/accueil.htm.

National indicators for all hospitals and for public reporting were built up to better inform the public and guide national and local policies. A first generation of five indicators were devised and released between 2005 and 2008, including 4 structures and process indicators and one outcome indicator.

Participation of hospitals to prevalence studies has dramatically increased over the years, from 830 hospitals in 1996 to 2337 (95% of all hospital beds) in 2006. The overall prevalence rate of all HAI was 4.9% in 2006. The adjusted prevalence rate of HAI (acquired in the hospital) recorded in the 1351 hospitals participating to both the 2001 and 2006 surveys decreased by 11%.

TABLE 1 - Comparison of surgical site infection rates recorded in 2004 in France, by comparison with European and US data.

	France ²	USA ¹	EU ²
Cholecystectomy	0.50	0.68	0.79 (0.50-8.85)
HIP replacement	1.88	0.86	1.41 (0.87-4.65)
Caesarian section	1.53	2.71	2.17 (1.03-6.85)
Colon Surgery	5.90	3.98	6.14 (2.21-14)
Coronary artery bypass	8.10 ³	3.39 ⁴	3.66 (2.85-9.04) ³

Data are provided as mean incidence rate of infection per 100 patients operated in 2004 within the NNIS 0 risk class, unless indicated otherwise.

¹Data from NNIS, 2004 (cdcinfo@cdc.gov)

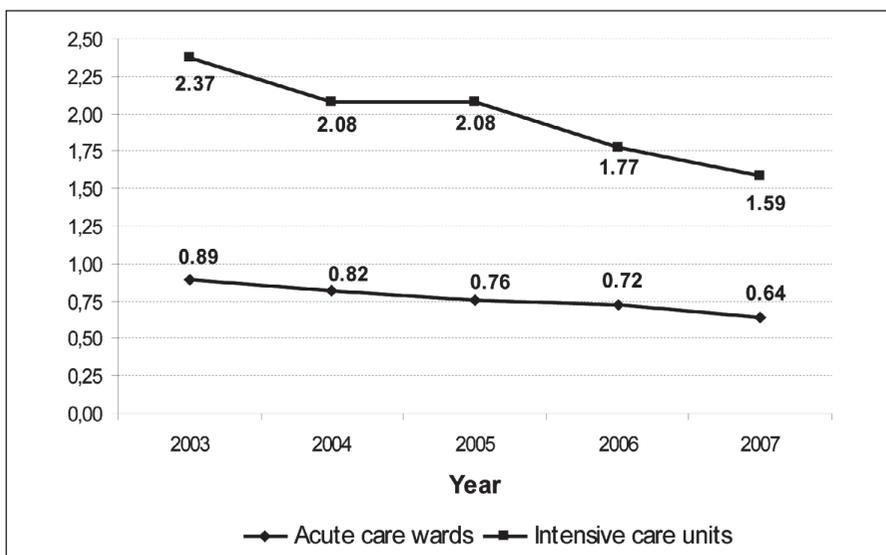
²Data from the European HELICS network, 2004, mean (range) (<http://helics.univ-lyon1.fr/>)

³Any NNIS risk strata

⁴median rates

Participation to the incidence networks also increased along time, with 25% to 35% of HCF participating to each one of the 5 surveillance networks. Data gathered along time within the networks are now used to build standardised infection ratios for infection surveyed, adjusted for risk factors and confounders identified within the patients and units records. For surgical site infections following scheduled surgery of low-risk classes procedures (NNIS risk classes 0-1), there was an overall decrease of infection rate by 25% between 2000 and 2005. Rates specific to interventions with highest volume are shown in the table, by comparison to those recorded in the US and in Europe.

FIGURE 1 - Trends in incidence density (cases/1000 patient-days) of clinical Methicillin-resistant *S. aureus* (MRSA) isolates in healthcare facilities (N=227) having participated since 2003 to the BMR-Raisin Network, by type of units, France, 2003-2007. (reproduced from ref. 1)



Data from several sources and networks concur to show that MRSA rates have decreased substantially in the past few years. In prevalence surveys, there was a 44% decrease of infections caused by MRSA (from 4.9/1000 patients to 2.9/1000 in 2001 and 2006, respectively). Data reported to the EARSS network also show an overall decrease of the median proportion of MRSA among all bacteraemic *S.aureus* isolates (from 33.4% in 2001 to 25.7% in 2007), whereas it had increased in most other European countries during the same period. Similarly, data recorded in the national MDRB network show a downtrend of MRSA incidence rate (from 8.9/10000 to 6.4/10000 patient-days between 2003 and 2007); this decreased was most apparent in intensive care units, where the control efforts have been initially focused (Figure 1). The 5 indicators for public reporting released progressively have provided a strong incentive to hospitals to strengthen their infection control organisation and activities. These include a composite score for organization, resources and activities implemented in the hospital by the infection control committee and infection control team, from which hospitals are ranked on a A to E scale, stratified by hospital category. This score has been released for the first time in 2005 (data from 2004 serving as reference year). From 2004 to 2007, the proportion of hospitals ranked A or B increased from 34% to 86%, with only 1% remained in class E by 2007. The other process indicators include the volume of hand-rub solutions used per year, targeting an objective based on a minimal number of handrubs per patient-day according to specialties in the hospital; a composite score for activities directed to good antimicrobial prescribing, and a scoring for surgical site infection surveillance. The fifth indicator relates to the incidence density of MRSA, for which the targeted goal was a 25% reduction within the period 2005-2008. This indicator has been released for the first time in early 2009 (2007 data), and only reports incidence density by hospital as a 3-year median rate without showing trends; this trend will appear in the next release. Very few national programs have been evaluated since the SENIC project. Although continuing efforts are required, the French program appears to have been effective at reducing infection rates and antimicrobial resistance.

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THE EXPERIENCES OF REGIONAL PREVENTION AND CONTROL OF BACTERIAL INFECTIONS AND ANTIBIOTIC RESISTANCE IN HOSPITAL AND IN THE AREA: LAZIO REGION

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In the past, prevention, surveillance and control of healthcare associated infections (HAI), in the Lazio region, Centre Italy, were characterized by sporadic and limited activities. Apart from the experience of the Comitato Cittadino established in 1994, which performed a prevalence study in 15 hospitals in Rome, available data derive from small and local experiences.

More recently, the “National Survey on the activities and control of hospital infections in public hospitals”, conducted by Istituto Superiore di Sanità (ISS) and the National Institute for Infectious Diseases (INMI) Spallanzani in 2000, showed a limited awareness of this problem in the policy of healthcare centres: Hospital Infection Control Committee (CIO) were present in 60% of centres vs 74% of the national average. In 2007, the Lazio Regional Council, under resolution 42, 25/01/2007, instituted the Regional Centre for the surveillance and control of HAI (CRIPA) entrusting its coordination to the IRCCS “Lazzaro Spallanzani” in cooperation with the Regional Public Agency for Health (ASP).

The CRIPA was designed in integration with the national, “Prevention and control of infections in health organizations and social health” (INF-OSS) program of the Ministry of Health. Priority areas for intervention in the CRIPA are to monitor the frequency of HAI, in particularly in surgery and intensive care unit, through prevalence and incidence studies; developing and sharing methods and techniques of auditing; control strategies, management of outbreaks and training of healthcare workers.

In 2007, it was conducted a survey in all regional public health facilities to collect data on existing programs of surveillance and control of HAI: on a total of 195 hospitals in the region, 60 answered to the questionnaire; of these, 53 reported to have a CIO.

In order to activate a laboratory-based, regional system of surveillance and alert the list of contacts for microbiology laboratories was defined and data on activities, systems and technologies in use, were collected. A total of 24 medium-high activity laboratories responded. In 5 laboratories has been launched, or it is in progress, the connection to the Micronet national network.

Educational and training activities were carried out at local and regional level: the number of CIO increased, accordingly.

TABLE 1 - Prevalence of surgical site infections (SSI) by procedure and NNIS risk index

Surgical procedure	Total number of procedures	N° SSI (%)	N° SSI (%) according to NNIS index category			
			M	0	1	2 + 3
Appendectomy	76	3 (3,9%)	0/11	2/51 (3,9)	1/5 (20%)	0/9
Cardiac surgery	110	2/110 (1,8%)	-	0/4	1/37 (2,7%)	1/69 (1,4%)
Cholecistectomy	430	8/430 (1,9%)	5/248 (2,0%)	1/141 (0,7%)	2/35 (5,7%)	0/6
Colon surgery	335	29/335 (8,7%)	0/4	5/80 (6,2%)	12/133 (9,0%)	12/118 (10,2%)
Cesarian section	858	29*/858 (8,4%)	0/2	20/647 (3,1%)	5/201 (2,5%)	1/8 (12,5%)
Hernia repair	262	1/262 (0,004%)	0/23	1/212 (0,5%)	0/27	-
Laminectomy	156	3/156 (0,02%)	0/3	1/75 (1,3%)	1/72 (1,4%)	1/6 (16,7%)
Breast surgery	404	9/404 (0,02%)	-	6/336 (1,8%)	3/65 (4,6%)	0/3

In April-June 2008 a surgical site infection (SSI) surveillance was conducted in 19 centers including 3 Research and 2 University hospitals. A database was created for the collection and analysis of data on antibiotic prophylaxis a finding not included in the Helics Win software. SSI were assessed according to the 1999 National Nosocomial Infection Surveillance (NNIS) system. Twenty interventions were monitored, (including caesarean section, cholecystectomy, colon interventions, mastectomy, laminectomy, hernia repair, cardiac surgery and appendectomy). On a total of 3059 interventions observed, the population was 27.5% men, and 72.5% women, with a median age of 60.5 and 37 (range: 1-96) years, respectively. Overall, the prevalence was 2.8, lower than corresponding national data (Table 1). Regarding the perioperative antibiotic prophylaxis, data have been analysed taking into account the National Guidelines (LG) issued in 2003 and in 2008. There was a general trend to use prophylactic antibiotics for all different types of intervention, including those in which the perioperative prophylaxis was not recommended by the LG; about the use of antibiotics, adherence to LG was low, ranging from 0% to 27.6%.

With regard to activities related to the control of epidemic events in healthcare facilities, 3 events were managed. The first was an hepatitis B (HBV) outbreak, which involved 3 patients with one death in a department of hematology. The epidemiological investigation conducted on a population of 48 subjects, allowed to identify the index case and the probable source in a non-disposable finger-stick device used for glucose monitoring; the attack rate was 6.2%. The second outbreak occurred in a department of hematology, involving 5 patients with 3 deaths. The

epidemiological investigation has involved a population of 16 subjects, and identified, as a likely source, the contamination of liquid soap with *P.aeruginosa*; the attack rate was 31%. In the third event INMI was called to provide support for the molecular identification of an epidemic strain of *A. baumannii* responsible for 9 concomitant cases of infection in a 12 bed intensive care. In all these three outbreaks, in addition to a classical outbreak investigation epidemiology, biomolecular methods were used and confirmed the clusters. Outbreak management allowed to update prevention measures and staff education.

Currently is in development the design of monitoring studies in intensive care and in long term care facilities (RSA), as well the participation to the WHO campaign 'Clean Care is Safer Care', aimed to promote hand hygiene in healthcare setting, also by using aqueous alcoholic solution, as the cornerstone of IPA prevention.

The experience so far developed has demonstrated the need for coordination of regional activities in order to standardize means and methods of control, and the importance of political and administrative commitment of the Management.

SIMPLE CRITERIA SUGGESTIVE FOR PULMONARY TB

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SENTILOMB AND BASALOMB PROJECT IN IRCCS HUMANITAS: AN HOSPITAL BENCHMARK WITHIN REGIONE LOMBARDIA

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Regione Lombardia (RL) created in 2002 CR-CIO (Decr. DGS n.8603 of 20.05.2002), a Regional Coordination of all Infection Control Units operating in each hospital within RL.

CR-CIO started 3 major surveillance activities on hospital's acquired infections, based on microbiology data:

- **SentiLomb project** to keep alert organisms under surveillance.
- **ResiLomb project** to monitor antibiotics resistance of *E.coli*, *P.mirabilis*, *S.marcescens* e *P.aeruginosa*.
- **BasaLomb project** to study *S.aureus* bacteraemia.

First project, started in 2004, become mandatory for all RL hospitals in 2006 (Circolare 8/SAN/2007). Private microbiology labs working with Regional Health System can also participate. IRCCS Istituto Clinico Humanitas joined SentiLomb project in 2006 and ResiLomb and BasaLomb project in 2007.

Aim of this work is to compare IRCCS Istituto Clinico Humanitas data to those produced by other RL's hospitals involved in these projects. Hospitals have been matched by number of beds and all data are analyzed by Regional Epidemiological Observatory.

SentiLomb

Alert organism	IRCCS Istituto Clinico Humanitas (Rate per 1000 admissions)	Other RL's Hospitals (Rate per 1000 admissions)	IRCCS Istituto Clinico Humanitas (Rate per 10000 days)	Other RL's Hospitals (Rate per 10000 days)
<i>S. aureus</i> (MRSA)	3.85	4.97	2.56	3.77
<i>S. maltophilia</i>	1.78	1.38	1.18	1.04
<i>E. coli</i> ESBL +	1.66	1.12	1.11	0.85
<i>Serratia spp</i>	1.26	1.21	0.84	0.92
<i>P. mirabilis</i> ESBL +	0.98	0.27	0.65	0.20

BasaLomb

<i>S. aureus</i> bacteremia	1.49	1.94	2.33	2.80
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These results show:

1. *S.aureus* resistant to meticilline (MRSA) is the most isolated alert organism in IRCCS Istituto Clinico Humanitas, at lower rates compared to other RL's hospitals.
2. *S.maltophilia* is our second most isolated alert organism.
3. *E.coli* ESBL+ is our third most isolated alert organism, with higher rates than RL's hospitals.
4. *Serratia spp* shows the same rate in our hospital and in RL's hospitals.
5. *P.mirabilis* ESBL + is our fourth most isolated sentinel germ, with higher rates than RL's hospitals.
6. *S. aureus* bacteraemia occurs in IRCCS Istituto Clinico Humanitas less frequently than in RL's hospitals.

This epidemiological pattern of alert organisms drive our hospital's Infection Control Unit to:

- Activate a specific surveillance program on MRSA carriers, before attending critical areas like ICUs or EAS.
- Implement control policies on *S. maltophilia* in ICUs.
- Perform a specific review program on antibiotic policies by reason of high rate of ESBL+ pointed out by Sentilomb project.

CLOSTRIDIUM DIFFICILE INFECTIONS IN A REHABILITATION WARD

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Clostridium difficile is an anaerobic Gram-positive bacterium which often causes antibiotic-associated diarrhea, mainly in hospitals.

The incidence of *Clostridium difficile* infections in a Rehabilitation ward during one year has been estimated. In 2008 232 patients have been hospitalized in the ward and ten of them (4,31%) have been affected by *Clostridium difficile* infections: 8 females, 2 male; average age: 61,8 (from 17 to 88).

Two of the patients came from Internal Medicine (one was operated on for a hip prosthesis, another one had hepatic disease due to alcohol abuse (HCV positive)), three from the Emergency Medicine (one with hemiparesis of the left side of the body, the other one, who had a syncope, with a heel fracture, the third, who had a serious injury with involvement of a lot of organs), three from Orthopaedics (that had fractures of the legs which had been operated on) one from his own home (who had his leg amputated) and one from Oncology (who had surgery on rachis osteocarcinoma).

Five of them already showed the infection when they were admitted in the ward, the other ones showed the symptoms only later.

The infections started in May and they have shown an increasing of their incidence in the last three months of the year: particularly in October (four cases). The patients showed these symptoms: temperature, diarrhea, stomach ache, asthenia.

All the patients have been treated with Metronidazole (250 mg, per os, 4 times a day) for ten days and hydration.

The necessary precautions have been used by the nurses and the physiotherapists who have been treating the patients; the relatives have been referred of the need of adopting precautions during the visits.

ESBL IMPACT IN THE HOSPITAL OF LODI LONG TERM CARE FACILITIES DURING 2008

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The risk of infection in long term care facilities (LTCFs) is increasing for different reasons: the greater circulation of multi drug resistant organisms (MDROs), patients transferred from the acute care to the LTCF setting and harboring multidrug-resistant bacteria, structural factors related to facilities, low-technology, understaffing and overcrowding. Early recognition and laboratory detection of MDROs may prevent multiplication and spread of such pathogens within LTCFs.

The present study reports the surveillance data about patients hospitalized in the Hospital of Lodi LTCFs during 2008; a microbiological analysis about the expanded spectrum beta lactamase (ESBL) - producing Enterobacteriaceae and the relative impact on these facilities was considered. 512 patients have been hospitalized during 2008 in four rehabilitation units: 2 devoted to geriatric rehabilitation (GR) and two to neuromotory rehabilitation (NR). Table 1 and table 2 report the epidemiological, clinical and microbiological data about the considered facilities.

TABLE 1

Ward	No. of Hospitaliz.	No. of Infections	No. of Infections			
			Pneumonia	C. difficile	Dec. ulc. ³	UTI
GR ¹	577	378	65	44	102	167
NR ²	512	52	2	4	7	39
TOTAL	1089	430	67	48	109	206

TABLE 2

Ward	Total No. of Hospitalization	Tot. No of ESBL	ESBL/ (%)
GR ¹	577	54	9.36%
NR ²	512	9	1.76%
TOTAL	1089	63	5.79%

Ward	Tot.No ESBL	ESBL UTIs	E. Coli		Klebsiella		Proteus	
			M	F	M	F	M	F
GR ¹	54	45	5	25	0	3	2	10
NR ²	9	10	2	2	1	2	1	2
TOTAL	63	55	7	27	1	5	3	12

GR¹: geriatric rehabilitation, NR²: neuromotory rehabilitation, ³decubitus ulcers

The UTI are the prevalent infections in the considered facilities especially in the geriatric rehabilitation wards.

This report underline the importance of improving the surveillance and control of infections in the considered LTCFs and the need of new strategies for prevention and early detection of ESBL.

The increasing problem of the general use of empirical antibiotic treatment for common infections such as indwelling catheter-associated UTIs, decubitus ulcers and pneumonia cause a rise of antibiotic resistant organisms in the long term care settings and further complicate the issue of infection.

INFECTION SURVEILLANCE IN RSA (NURSING HOME) PATIENTS

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Elderly patients are exposed to infections, due to their anatomical, physiological and functional characteristics, especially when institutionalized or in hospitals. Well-known risk factors for nosocomial infections are comorbidity, functional and cognitive impairment, pressure ulcers, invasive devices. These are common features in RSA (nursing homes) residents, so that one can expect to find some occurrence of infections. The RSA at Istituto P. Redaelli in Milano (about 300 beds) contains most of all very old patients (average age 83), dependent in basic ADL, with elevated medical complexity, often cognitively impaired. Besides, inside this RSA there are a 40 beds ward for patients with severe cognitive impairment and behavioural disturbances (NARSA) and a 12 beds unit for patients in vegetative state (SVP). In order to test the stated hypothesis we performed a longitudinal study on 3 units: one RSA unit with 46 beds (3PR), an Alzheimer ward (NARSA) and the SVP unit. The study lasted 1 year (from Jan. 1st to Dec. 31st 2008). To detect diagnosis of infections we used the Mc Geer criteria for infection surveillance in long term care facilities. The criteria have been modified for SVP patients, since they are not able to explain subjective symptoms. The results of the identifications of pathogens in all the samples sent to the microbiology lab of the Istituto by the 3 units all the year long, have been recorded. The incidence in 3PR was 45 events in 16481 patient-care days (2,73/1000 days); in NARSA it was 53 events in 14997 days (3,53/1000); in SVP 39 episodes in 3329 days (11,72/1000). It is important to stress that in all 3 areas more than 50% of the events consisted of lower respiratory infections: 65% in 3PR, 53% in NARSA, 58% in SVP. As a second more frequent infection in NARSA and 3PR, skin/soft tissues/wound (CTF) infections, respectively 26% and 16%. Only in SVP the second infection was UTI (28%) and the third was CTF with 10%. 46 strains of pathogens were isolated in 3PR, 20 in NARSA and 128 in SVP. In 3PR 63% of the isolates were enterobacteriaceae (basically E.coli and Proteus mirabilis); nearly the same in NARSA (65%); in SVP Enterobacteriaceae were 41%, Pseudomonas aeruginosa 14%. The most relevant results in spectrum of resistance of the isolates show a strong presence of ESBL+ in SVP (100% of E.coli and 90% of Proteus mirabilis). The evidence of carbapenem-resistant Pseudomonas aeruginosa in SVP (28%) is particularly interesting.

In conclusion, infections in nursing homes are a relevant aspect, particularly amongst patients at higher risk, so that it becomes one of the major clinical problems in SVP patients. Also the occurrence of multi resistant pathogens, representing a typical hospital flora, is related to a higher risk.

BIOFILM FORMATION AND AGGREGATIVE ADHERENCE OF BETA-LACTAMASE PRODUCING *PROTEUS MIRABILIS* CLINICAL ISOLATES IN ITALY

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Objectives: Urease-producing *Proteus mirabilis* colonizes the catheter surfaces forming extensive biofilm communities and causing infection. UTI may become chronic, with a microbial persistence may be due to both antibiotic resistance and adhesion. We investigated biofilm formation and aggregative adherence of *P. mirabilis* TEM-92 and CMY-16 producers.

Methods: 20 isolates of *P. mirabilis* collected during 2003-2007 from 2 Italian hospitals and from 1 nursing home, susceptible to imipenem (IMP) and piperacillin/tazobactam (TZP) including CMY-16 and TEM-92 producers and beta-lactamase (BL) negative strains, were examined for biofilm formation. Crystal violet assay was performed in different culture conditions and in presence of IMP or TZP sub-MIC concentrations. The presence of *mrpA* gene encoding for the major fimbrial subunit of MR/P fimbriae was investigated by PCR. 4 selected strains were also tested for adherence to LLC-MK2 epithelial cells grown on a coverslip.

Results: All strains resulted proficient in biofilm formation especially in urine. Biofilm formation was similar for CMY-16 and TEM-92 producers; a fewer biofilm formation was observed in BL negative strains. Sub-MIC concentrations of IMP and TZP stimulated biofilm increase in all strains. *mrpA* gene was detected in all strains; the 4 strains studied for adherence to LLC-MK2 showed few bacteria forming aggregates in intercellular spaces and 75% of bacteria adhered to the coverslips after 1 h of incubation; after 4 hrs great adherence in intercellular spaces and few bacteria on cells were observed. We found differences in arrangement on coverslips among the 4 strains tested.

Conclusions: All BL producers, regardless of the enzyme type, resulted equally proficient in biofilm production, that increased in presence of sub-MIC concentrations of IMP and TZP; the BL negative strains showed a low ability to produce adhesion factors. Cellular adherence assays showed preferential adhesion to inert surfaces rather than to epithelial cells. Although the results didn't fully support a direct correlation between BL production, biofilm and persistence, both these mechanisms contribute to UTIs cronicization.

INCREASING INCIDENCE OF LISTERIA MONOCYTOGENES MENINGITIS IN EAST EMILIA

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Background: *Listeria monocytogenes* is a facultative intracellular bacterium that has predilection for causing central nervous systemic infections especially in immunocompromised patients. Host factors that increase the risk of listeria infection are: pregnancy, acquired immunosuppression, haematological malignancies, diabetes mellitus, renal failure and chronic alcoholism. In some European countries the incidence of listeriosis has increased. In Northeastern Italy the incidence of the disease with cerebral involvement is underestimated since it's unsuspected.

Objective: To study the incidence, epidemiological and clinical features of meningitis due to *Listeria monocytogenes* in East Emilia.

Methods: We have analyzed by means of computed database all the cases of acute meningitis in HIV negative patients admitted to our Department of Infectious Diseases between January 1989 and December 2008. Demographic data, predisposing conditions, underlying diseases, CSF cell count, CSF chemical data, CSF bacterial antigens, CSF and blood cultures, clinical therapeutic features and outcome were investigated with an accurate flow - chart. The diagnosis of listeriosis was confirmed by the National Reference Center for Listeria, Institut Pasteur, Paris (France).

Results: During the study period, 183 cases of meningitis have been observed: 91 with purulent CSF and 92 with clear CSF; ratio males/females 1,4; median age 53,5 years patients with purulent CSF and 46,5 years patients with clear CSF (range 16 - 88). The study was divided in four compared periods: 1989-93, 1994-98, 1999-2003, 2004-2008. The incidence of listeria infection has been increased: from no cases in the first period, 4,4% in the second, 6,7% in the third and 19% in the last period. The incidence for 100.000 persons in the same periods was respectively: none, 0,28, 0,57 and 1,14. Risk factors of the 7 observed cases were: chronic alcoholism, haematological malignancies and advanced age. Clinical features were: fever, confusion, rigor, headache and indisposition. 6/7 cases showed purulent CSF with cell count between 700 and 2500/mmc. The last three observed cases presented *in vitro* resistance to ampicillin, so was employed levofloxacin *i.v.* in association with ceftriaxone. Two patients developed hydrocephalus.

Conclusions: The meningitis due to *Listeria monocytogenes* is increased in our area. This pathogen can be found in the food supply and most infections are acquired through ingestion of contaminated food. This is an important vehicle in order to high rate of isolation (17,4%) in soft cheese, vegetable and chicken. The increased incidence of CNS listeriosis especially among persons >60 years of age make indispensable an empirical therapy with a drug active against *Listeria monocytogenes*.

AUDIT ON HIGH COST ANTIBIOTICS USE IN A DEPARTMENT OF INTERNAL MEDICINE: A PRELIMINARY REPORT

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Background: Increasing rates of resistance to antimicrobials among hospital pathogens is a worldwide problem that has been recognized for more than twenty years. The consequences of resistance are well known, including increased morbidity, mortality and costs of healthcare. Inappropriate antibiotic use is recorded in 25-50% of hospital prescriptions. Antibiotic misuse is common in empirical and targeted therapy. The major reasons for inadequate therapy are the use of antibiotics with unnecessarily broad spectrum and longer than needed duration of therapy. Many clinicians have a limited perception of the problem of antimicrobial misuse and resistance therefore multiple strategies have been developed to optimize the therapeutic management. In our Department of Internal Medicine during the 2007 the cost DDD of antibiotics was 4,86 respect to 4,13 of the previous years.

Objective: To evaluate the appropriateness of high cost antibiotics use in a large department of internal medicine of an University Hospital of North Italy.

Methods: A retrospective audit was performed between may and december 2008 to analyze antibiotics treatments with piperacillin – tazobactam, meropenem, teicoplanin and linezolid in hospitalized patients in the 2007. The study was carried out by reviewing all medical records of patients who received one or more of the antibiotics about reported. The appropriateness of the treatments was studied with regard to the bacteriological results, serious infections, risk factors, multiple morbidity and previous failures.

Results: 146 high cost antibiotic prescriptions of 110 patients were analyzed during the study period. 81,5% of prescriptions were appropriate with regard to the criteria used. Piperacillin/Tazobactam and Meropenem were used often as etiologic therapy. The rate of inappropriate teicoplanin use was of 28,8%.

Conclusions: This audit conducted in a department of internal medicine reveals that the appropriateness of high cost antibiotics prescriptions was significantly higher if compared with other as surgical wards. Antibiotics against gram negative were adequate. An important rate of inappropriate high cost antibiotic prescriptions was observed for teicoplanin, confirming the need to develop control strategies regarding the utilization of antibiotics in order to control the diffusion of multiresistant bacteria. The informations obtained of our audit may to improve the appropriateness of antimicrobial therapy in the internal ward with reduction of the mortality.

ACTIVE SURVEILLANCE OF MRSA IN ICU

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Objective: The aim of this work was to study the acquisition and cross-transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) in Intensive Care Unit (ICU) of A.O. Fatebenefratelli of Milan and their antimicrobial susceptibility pattern.

Methods: Between February and May 2007, all patients hospitalized >48 hrs in the ICU had nasal swab specimens obtained at admission and weekly during their stay. Identification of *Staphylococcus aureus* was confirmed by standard methods and the antimicrobial susceptibility testing was performed by Kirby Bauer, Etest and microdilution method. Interpretation criteria were those of the CLSI.

Results: A total of 233 patients were admitted to ICU, 38 (16,3%) of these patients were found to be colonized with MRSA at least once during ICU stay (19 at admission and 19 acquired). Five patients (2,1%) achieved a MRSA infection during the study period. Out of 38 strains of MRSA isolated from clinical and screening samples, more than 65% were found to be resistant Ciprofloxacin, Gentamicin and Tobramycin. D-Test performed with Erythromycin (E) and Clindamicin (CC) disks showed 18/38 strains (47,4%) with constitutive resistance to MLS antibiotics (E=CC=R), 7/38 strains (18,5%) with inducible resistance (D-Test +), 5/38 strains (10,5%) with resistance mediated by an efflux mechanism (E=R,CC=S). Thirty-four of MRSA tested (89,5%) were susceptible to Rifampicin and 31 (82%) were susceptible to Tetracycline. All MRSA strains were sensitive to Linezolid (MIC₅₀ 0,75mg/ml; MIC₉₀ 1 mg/ml), and Daptomycin (MIC₅₀ 0,094 mg/ml; MIC₉₀ 0,64mg/ml). No strains were resistant to Vancomycin (MIC₅₀ 1,5 mg/ml; MIC₉₀ 2 mg/ml) and Teicoplanin (MIC₅₀ 1,5 mg/ml; MIC₉₀ 4 mg/ml).

Conclusions: To reduce the prevalence of MRSA, the regular surveillance of hospital acquired infection, isolation nursing of carriers for MRSA, monitoring of antimicrobial susceptibility pattern and formulation of a definite antibiotic policy may be helpful.

ANTIRETROVIRAL THERAPY IN AIDS PRESENTERS OBSERVED AT LEGNANO GENERAL HOSPITAL (ITALY) DURING THE PERIOD 2000-2008

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Rationale: 10% to 30% of HIV patients in Northern countries still present late for care, when CD4 cells are <200 cells/mcl and symptomatic HIV disease has occurred. The outlook of these patients is very much dependent upon the initial response to ART, but even if optimal response to treatment has been achieved, long-term prognosis may be impaired.

Objectives: To describe trends over time from January 2000 to December 2008 in AIDS presenters diagnosed in Legnano (Italy), to describe their clinical and immunological characteristics and evaluate initial response to ART.

Methods: 76 AIDS presenters (48,7% of all new AIDS diagnoses in the study period) were included. We examined factors associated with being a late presenter, defined as individuals presenting with CD4 cell count <200 per mcl or AIDS within 1 month of their anti-HIV Ab positive test.

Results: The proportion of AIDS presenters (Ap) increased significantly over time ($p < 0.001$).

Sexual transmission was the major risk factor for AIDS presenting, while male or female sex was not a determinant. At the time of diagnosis, median of CD4 cells was respectively 88 and 70 per mcl in AP and non Ap group, and HIV RNA log was 5,24 and 5,29 respectively. 15 AP die by AIDS-defining diseases, 7 were early dropout within first month of therapy. The remaining AP started an ART at the diagnosis, meanly with 2NRTI + 1 boosted PI (72%). A drug resistance genotyping test was performed in 40% of patients (quite systematic from May 2005). Median duration of initial ART was 107 days, and discontinuation was mainly due to adverse events or simplification. At 3 months, 34% had undetectable HIV-RNA, median HIV-RNA log was 2,24 and CD4 cell count was 140. At 12 months, 84% had undetectable HIV-RNA, with a median CD4 cell count of 310.

Discussion: As expected in the HAART era, a substantial proportion of our AIDS presenters are maintained in immuno-virological response in the study period.

PHENOTYPIC AND GENOTYPIC CHARACTERIZATION OF INVASIVE *STAPHYLOCOCCUS AUREUS* ISOLATES IN ITALY

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Objectives: As methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the leading causes of morbidity and mortality in hospital settings we examined nosocomial invasive *S. aureus* strains in order to characterize them both microbiologically and epidemiologically by phenotypic and genotypic methods.

Methods: In the period 1 September 2006 - 28 February 2007, 147 invasive *Staphylococcus aureus* strains were obtained from 19 hospital laboratories distributed all over the country. Susceptibility to antibiotics were assayed by automated systems; MICs to glycopeptides were confirmed by E-Test. CLSI breakpoints were applied. The *agr* group and the SCCmec were determined by PCR. The repeat region of the *S. aureus* protein A (*spa*) gene was sequenced and analysed by the Ridom Staph Type software. MLST was also performed.

Results: Out of 147 isolates, 81 were MSSA and 66 MRSA. By automated system all the isolates were susceptible to vancomycin, teicoplanin and linezolid. Resistance to ciprofloxacin, erythromycin, gentamicin, clindamycin and rifampin was found in 45%, 38%, 33%, 33% and 9% of the isolates, respectively. 4% of isolates was found resistant to tetracyclin; By E-Test vancomycin susceptibility for MSSA was: MIC₅₀ = MIC₉₀ = 1.5 mg/L; for MRSA: MIC₅₀ = 1.5 mg/L, MIC₉₀ = 2 mg/L. Only among MRSA, 3 strains were VISA (MIC = 3 mg/L). By *spa* typing, MSSA were highly heterogeneous. Among MRSA three main groups were identified: t041(23 isolates), t008(19 isolates) and t001(9 isolates). Out of 3 VISA, 2 were assigned to *spa* type 041. All the isolates assigned to *spa* type 041 harboured SCCmec type I and *agr* 2. By MLST, selected strains among those characterized by *spa* type 041, including one VISA strain, belonged to clonal complex (CC)5.

Conclusions: Most invasive *S. aureus* Italian isolates showed reduced susceptibility to vancomycin. Among MRSA, 3 VISA strains emerged and *spa* type t041 was the most frequent nosocomial *spa* type.

FIRST REPORT ON *K. PNEUMONIAE* STRAINS PRODUCING BOTH VIM AND CTX-M TRANSFERABLE ENZYMES

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Objectives: The recently reported emergence of carbapenem resistance among metallo- β -lactamases (MBLs)-producing *Enterobacteriaceae* is a matter of clinical concern.

The aim of this study was to screen for the presence of beta-lactamases among *Klebsiella pneumoniae* clinical isolates showing reduced susceptibility to carbapenems.

Methods: During the period 2007-2008, 30 *K. pneumoniae* isolates with reduced susceptibility to carbapenems were collected from a Rehabilitation Facility located in Pavia, and two acute care hospitals, one placed in the same city and the other in S. Giovanni Rotondo. MBL and Extended-Spectrum β -lactamases (ESBLs) production were screened by the use of IPM-EDTA and double disc synergy tests, respectively. Imipenem (IPM) MICs were determined by both E-test and broth macrodilution methods (CLSI 2008). Isoelectric focusing (IEF) was performed with crude cell extracts of all the potential ES β L producers. The β -lactamase genes were identified by PCR and sequencing. Genomic DNA, digested with XbaI, was subjected to PFGE. MBL and ESBL genes transferability was investigated by conjugation and plasmids were characterized by RFLP analysis.

Results: The IPM-EDTA disc synergy test yielded a positive result in 14/30 strains, characterized by IPM MICs ranging from 2 to 128 mg/L. PCR experiments detected *bla*_{VIM-1} like genes in the same 14/30 isolates. The sequenced *bla*_{VIM-1} gene was located on a conjugative plasmid; *bla*_{SHV-5} and *bla*_{CTX-M-1} genes resulted co-transferred in 11/14 and 3/14 cases respectively.

VIM-1 producers were revealed in all hospitals. Two clones were detected, both responsible for outbreaks. The clonally related *K. pneumoniae* isolates collected from 6 different wards of the Pavia acute hospital harboured different conjugative plasmids 80-90 kb large; an identical conjugative plasmid 85 kb large was while characteristic of the strains from the S. Giovanni Rotondo hospital ICU.

Conclusions: This is the first report on the emergence of a MDR clone of *K. pneumoniae* producing VIM and CTX-M transferable enzymes.

Control measures including screening by IPM-EDTA synergy tests should be routinely applied to detect MBL producing strains and to contrast the vertical and plasmidic diffusion of carbapenem-resistant *K. pneumoniae* in acute care and rehabilitation facilities.

SURVEILLANCE OF URINARY TRACT INFECTIONS IN THE ELDERLY: A STUDY OF INCIDENCE

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In October 2008 we began a 6-months Study of Incidence at the Long-Term Stay Hospital ("Villa Beretta") and three departments affiliated to our hospital. The hospitalized patients in the study suffer from serious clinical diseases (brain-damage, myelin lesions, respiratory problems, post-acute stroke).

The aim of the study was to describe the rate of incidence of urinary tract infections, to evaluate the frequency of isolated organisms and to identify the risk factors for nosocomial infections (NI) of the urinary tract.

The study involved different health professionals each with precise assignments: "Comitato Infezioni Ospedaliere" (C.I.O.) (responsible for study development), Sanitary Coordinator (responsible for transmission of data to all operational units), nurses responsible for Infection Control (I.C.I.) (coordination among the different operational units), doctors and nurses responsible for departments (compilation of questionnaires) and microbiologists (control and elaboration of data).

The data were processed with VIGI@CT software (bioMérieux), used for data handling of epidemiological-studies, control and monitoring of NI and germ surveillance including Multi-Drug Resistant Bacteria (MDRB).

The software is connected both to the LIS of the laboratory and to the automated system for the identification and the assay of antibiotic sensitivity in use in our laboratory (VITEK 2 Compact, bioMérieux); from the LIS it draws patient data (name, sex, date of birth, date of admission) and the type of sample from which to seek possible germ "alert". While from the VITEK 2 it receives the specifications of the isolated germ (identification and pattern of antibiotic sensitivity).

In the four months prior to the Study of Incidence, we verified the correct operation of the VIGI@CT software with the LIS and VITEK 2 data, to recognize and to alert the types of resistance that we wanted to keep under control and to associate the suspected NI with the relative questionnaire.

According to our criteria related to the times of onset of the infection (e.g. 48 hours from date of admission), antibiotic sensitivity and/or monitoring of the germ surveillance, the VIGI@CT associates with each patient the germ/s that has/have the characteristics to cause infection, and it automatically prints the suspected NI and/or the germ alerted and a related questionnaire.

The printed report is sent daily to the involved departments via courier who will also take the filled questionnaires back to the laboratory within 48-72 hours in case of a suspected hospital infection for elaboration of data.

The notification of the germ alerted is handled by doctors and nurses responsible for the department or by I.C.I. with the aim of controlling the spread of infection.

Data from the questionnaires are entered into the VIGI@CT program and analysed with the aim to establish if the isolated germ is responsible for NI.

We present data from the first three months of the study, with the aim to have a preliminary view of the incidence of urinary tract infections defined as nosocomial, of the circulation of microorganisms and above all of the incidence of MDRB.

To date we found an almost complete correspondence between the suspected NI notified by the software and the questionnaire filled by the referent doctors.

The small discrepancy between the number of confirmed microorganisms responsible of NI and the number of isolates per department, is due to the software command that makes an isolated microorganism responsible of a second infection for the same patient only if at least 15 days have elapsed from the previous alert.

MEASLES OUTBREAKS IN A NORTHERN ITALIAN AREA FROM 1997 TO 2008: EPIDEMIOLOGY AND VACCINE COVERAGE

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Measles, in spite of available vaccination, remains a heavy public health burden worldwide. In Europe in 2006 and 2007 several countries have reported high numbers of cases and outbreaks.

Lodi, a Province located in the south of the Lombardy Region with 227,000 inhabitants, has also been affected by this hyper-endemic for measles.

The aim of this study is to describe three measles outbreaks occurring during the period from 1997 to 2008 in the Province of Lodi to analyse the epidemiological characteristics and assess the corresponding immunization coverage.

We reviewed each case diagnosed and notified the local Health Authority regarding age, residence, immunization status, hospitalisation and, if available, laboratory confirmation.

Only for the third outbreak was each case investigated by phone and for the most part laboratory confirmation was possible.

Results: The outbreak of 1997 reported 159 cases involved, the median age was 13 years; the largest number of cases was in the population under 20 years with 37.7% <11 years and 41,5% between 11–19. In that year, local vaccine coverage for one dose at 24 months was 64%, at 10 years it was about 40% and at 11 years about 68%. The second outbreak occurred between 2002 and 2003 with 128 cases: the median age was 8.5 years and children aged <11 years were the most frequently affected (78%); the immunization coverage for one vaccine dose at 2 years was 81% while at 10 years it was 63%; the area with the lowest immunization rates in the Province had the most number of cases.

The last outbreak occurred in 2008 with 31 confirmed cases. The median age was 20 years, the age-group most represented was 20-31 years with 15 cases (42%). The vaccine coverage for one dose at 2 years was 96.6% and at 10 years was 94%.

Conclusions: The population aged between 18 - 40 is the most vulnerable to measles; the high immunization coverage of subjects up to 18 years substantially eliminates their susceptibility, while subjects >40 years are no more susceptible.

These data confirm the effectiveness of vaccination and of the vaccination strategy adopted in our territory.

INCREASING OCCURRENCE OF PLASMID-MEDIATED AMPC BETA-LACTAMASE PRODUCING PROTEUS MIRABILIS CAUSING BLOODSTREAM INFECTIONS

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Background: Plasmid-mediated AmpC beta-lactamases (CBLs) have been increasingly reported over the last few years. However, prevalence and distribution of CBLs among enterobacteria are still largely unknown. The aim of this study was to evaluate the CBL production in blood culture isolates in comparison with the production of extended-spectrum beta-lactamases (ESBLs).

Methods: Enterobacteria obtained from blood cultures performed at the Manzoni Hospital (Lecco, Italy) during a 5-year period (2004 to 2008) were included in the study. Identification and antimicrobial susceptibility were carried out using the VITEK 2 instrument (bioMérieux). ESBL and/or CBL production were assessed according to CLSI criteria (when available) and confirmed by molecular methods.

Results: Overall, 45 ESBL-positive isolates were detected, including *Escherichia coli* (n=29), *Proteus mirabilis* (n=5), *Klebsiella pneumoniae* (n=5), *Enterobacter cloacae* (n=2), *Enterobacter aerogenes* (n=2), and *Serratia marcescens* (n=2). No significant differences were observed over the years (2004, n=5; 2005, n=10; 2006, n=11; 2007, n=11; 2008, n=8). On the contrary, CBL production was detected solely in *P. mirabilis* isolates (n=6), starting from February 2007 from a neurosurgical patient. The remaining 5 isolates were collected from February to August 2008 from patients admitted to different wards. Carbapenems (ertapenem, imipenem, and meropenem) and amikacin were consistently active against both ESBL- and CBL-positive isolates.

Conclusions: *P. mirabilis* isolates producing CBLs have emerged among enterobacteria causing bloodstream infections in our hospital. Together with ESBL-producing enterobacteria, they represent a new challenge for physicians and microbiologists. Carbapenems and amikacin show potent *in vitro* activity against both ESBL- and CBL-positive isolates thus representing a valid therapeutic option for treating infections caused by these MDR pathogens.

MOLECULAR CHARACTERIZATION OF STRAINS OF CLOSTRIDIUM DIFFICILE ISOLATED FROM HOSPITALIZED GERIATRIC PATIENTS

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Introduction: *Clostridium difficile* (Cd) is a spore-forming, gram positive anaerobic bacillus. It can be found as commensal in the human intestinal flora. Cd is the etiologic agent of pseudomembranous colitis and the most common cause of nosocomial antibiotic-associated diarrhea. The pathogenic strains produce toxins (A and B) with cytotoxic effects on intestinal epithelium. Some strains producing binary toxin, cause more severe infections. So far it is not known the specific role of this toxin.

The major risk factors for acquiring this infection are: advanced age (over 65), underlying disease, severity of illness, antibiotic exposure and prolonged hospitalization. The purpose of our work was to perform a molecular characterization of Cd strains isolated from patients hospitalized at ASP Pio Albergo Trivulzio. We also performed the analysis of sequential isolates in order to verify if the recurrent infections were due to relapse or reinfection.

Methods: A total of 100 C.d. isolates were collected from 75 symptomatic patients from 6 different hospital wards. The strains were cultured on blood agar plates (CD agar - bioMérieux) in an anaerobic atmosphere for 48 h at 37°C. The identification of species was performed using Vitek automated system (bioMérieux).

The molecular typing was performed by “ribotyping” according to the method described by Bidet et al., using the 16 S (5'-GTGCGGCTGGATCACCTCCT-3') and 23 S (5'-CCCTGCACCCTTAATAACTTGACC-3') sequences. Furthermore, all strains were subjected to PCR to detect the presence of the gene coding for binary toxin.

Results: The analysis of patterns obtained by ribotyping showed 14 different ribotypes. None of the strains tested was found to produce binary toxin.

Conclusions: The data obtained indicate that there is a considerable spread between the same ward in respect of the spread between different wards. For this phenomena we can assume that the spread has been fostered by the movements of patients in different rooms and that the environment is a possible source of infection. Most of the sequential samples belong to the same ribotype indicating that the recurrent infections may be due to relapse from treatment failure or reinfection with the same strain. The lack of toxin-producing strains binary allows for the time being, not to further increase the rate of mortality.

EFFECT OF CMV-IMMUNOGLOBULINS (CYTOTECT BIOTEST) PROPHYLAXIS ON CMV PNEUMONIA AFTER LUNG TRANSPLANTATION

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Introduction: Lung transplant (LT) recipients among solid organ transplant recipients are at high risk for cytomegalovirus (CMV) infections. The clinical symptoms related to CMV disease and the prevention of CMV infection show variation among different patient populations, depending on the type of transplant and the intensity of immunosuppression. The two main approaches for prevention of CMV disease are prophylaxis and preemptive therapy with currently available antiviral compounds. We evaluated the effect of CMV-Immunoglobulins (CMV-IG) (Cytotec Biotest) on CMV pneumonia diagnosed in 303 follow-up transbronchial biopsies (TBB) of lung transplant recipients.

Methods: At our Centre 24 patients (control group, 155 TBB from 1999 to 2002) received acyclovir for 24 months and 33 recipients (study group, 148 TBB from 2003 to 2008) received a combined CMV prophylaxis consisting of CMV-IG (Cytotec Biotest) at day 1,4,8,15,30 and monthly for 12 months and a short Ganciclovir or Valganciclovir therapy from 21th postoperative day for 3 weeks followed by acyclovir up to 24 months. Statistical analysis was performed using Chi-square test for proportion differences.

Results: In our study the percentage of pneumonia at first month TBB was similar in study group vs control group, 9.1% (3/33) vs 8.3% (2/24), p=0.9 ns, but after the first month the percentage was significantly lower in study group in first year at follow-up TBB (months 3,6,9,12), 1% (1/99) vs 6.4% (5/78), p=0.048, and in first two years follow-up TBB (months 3,6,9,12,18,24), 0.8% (1/122) vs 6.5% (8/124), p=0.018.

Conclusions: Our data suggest a strong efficacy of CMV-IG prophylaxis in reducing CMV pneumonia after first month in lung transplant recipients. The effect of first year post transplant combined prophylaxis seems to be useful in preventing not only first year but also second year CMV pneumonia suggesting some long lasting immunological role of prophylaxis that needs more studies to be better defined.

A SURVEY THE SURVEILLANCE OF NOSOCOMIAL INFECTIONS IN THE PROVINCE OF VARESE: RESULTS AND PERSPECTIVES

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In January 2008 the Local Health Unit of the Province of Varese (ASL) promoted a survey about nosocomial infections surveillance and control systems (NISCS), involving all public and private accredited hospitals.

A questionnaire was compiled by the nine company hospitals (17 centers) of the province of Varese. The results show some critical point such as the still meager spread of guidelines related to the prevention of fecal-oral transmitted infections or in transplanted/ immunocompromised patients. So are the guidelines regarding the prevention of infections from incoming/outcoming patients from other departments/ structures and the profitable systems of sentry events. As for the composition of NISCS commissions, the occupational health specialist is present only in 50% of the structures questioned, the microbiologist and infectivologist respectively in 71% and 43%.

After the presentation of the results to the structures interested and the discussion that followed, three work groups were constituted under the coordination of ASL Bureau Authorization and Accreditation of the Health Structures, composed by personnel from ASL and hospitals, with the aim to propose documents and guidelines to be shared on the following themes: the hygiene of the hands in preventing hospital infections; antibiotic choices for hospital infections preventions and monitoring of the antibiotic-resistances; the prevention of “import-export” infections both inside the hospitals and in health and social structures (a still little explored topic which is worthy of deepening).

In preparing local operational protocols particular attention will be paid to indications coming from the most updated science literature.

EMERGENCE OF PANTON-VALENTINE LEUKOCIDIN POSITIVE COMMUNITY-ACQUIRED MRSA (PVL+CA-MRSA) AND MSSA (PVL+CA-MSSA) INFECTIONS IN AN ITALIAN HOSPITAL

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Objectives: The worldwide emergence of CA-MRSA infections caused by hypervirulent strains producing PV leukocidin (PVL, coded lukS-lukF) is a problem of extreme interest. Molecular studies suggest a spread of a limited number PVL-producing MRSA clones that are genetically distinct from hospital-acquired strains. This emergence of PVL+ CA-MRSA represents a public health threat, because these strains are associated with severe soft tissue infection and necrotising pneumonia. In this report the Authors describe 3 cases of PVL+CA-MRSA and 1 case of PVL+CA-MSSA infections observed in 2008.

Methods: *Staphylococcus aureus* (Sa) isolates in Mantova hospital (530 beds) were identified by conventional tests, followed by the determination of MIC for Oxacillin by the agar dilution method. The presence of lukS and lukF genes (encoding PVL) were defined by PCR at the National Institute of Health (Istituto Superiore di Sanità) in Rome.

Results: A total of 348 *S. aureus* isolates were collected from different patients during 2008. Among them 97 (27.9 %) were MRSA and 251 (72.1%) were MSSA. Three MRSA cases were PVL+ and also 1 MSSA case was PVL+. 2/3 cases of CA-MRSA were associated with skin and soft tissue infection and 1/3 case was sepsis complicated by meningitis and brain abscess. The case of PVL+CA-MSSA was associated to the cervical spondylodiscitis. Every patient was positive for Sa oro-nasal carriage. In just one case of PVL+ CA-MRSA there was a recent history of hospitalisation. No case of staphylococcal infection was reported among the relatives or close social contacts. The cases were resolved thanks to a treatment with glycopeptides, but one case required linezolid therapy.

Conclusions: Specific surveillance of MRSA and MSSA infections in the community is required to monitor and prevent the spread of these PVL+ strains. The alert system and the control of the local epidemiology of PVL+ CA-MRSA/MSSA represents a priority even in small hospitals.

STAPHYLOCOCCUS AUREUS: A RETROSPECTIVE EPIDEMIOLOGIC STUDY BETWEEN 2004 AND 2008 AT IRCCS POLICLINICO SAN DONATO (MILAN)

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Objective: The aim of this study was to characterize the methicillin-sensitive (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) strains obtained at the Clinical Microbiology Laboratory of San Donato Hospital, 2004 to 2008.

Method: Bacterial strains were isolated from different clinical materials (surgical wound, respiratory material, blood cultures in predominance); *S. aureus* identification and susceptibility testing were assessed by the StaphID32 API system (Biomérieux); the phenotypes of resistance were confirmed with disc diffusion and E test for methicillin. Genotype of MRSA from blood cultures was performed with PCR (Zhang method).

Results: *S. aureus* was isolated from 2247 specimens of which 1063 (47%) were resistant to methicillin and 1184 (53%) were sensitive to methicillin. MRSA represented 82% of all from respiratory material, 52% from blood cultures and 40% from surgical site. No *S. aureus* was found resistant to Vancomycin. 17 blood cultures MSSA (19%) were susceptible to all the antibiotics. All blood cultures MRSA were resistant to Penicillin and showed a predominant antibiotype (58%) with resistance to Gentamicin, Erythromycin, Clindamycin and Norfloxacin. Susceptibility testing of blood cultures MRSA indicated that over 94% of MRSA were resistant to Erythromycin and 81% were resistant to Clindamycin. Oxacillin resistance was confirmed by the detection of the *mecA* gene. Zhang genetic type I was the most commonly (about 75% of isolates) from blood cultures MRSA, followed by type II (about 25%).

Conclusions: Continuous surveillance on resistance patterns of *S. aureus* in understanding new and emerging trends is of utmost importance. Traditional and SCC*mec* typing methods in contemporary represent important tools to classifying strains and to understand the epidemiology and evolution of MRSA.

DETECTION OF EBV IN BRONCHOALVEOLAR LAVAGE FROM LUNG TRANSPLANT PATIENTS

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Rationale and aims: The lower respiratory tract is a latency site of EBV, however its pathogenic role is poorly known, particularly in transplant patients. The aim of this study was to evaluate the prevalence and role of EBV in lung transplant vs other transplants.

Methods: EBV-DNA was detected by Real Time PCR in 108 bronchoalveolar lavages (BAL) from 60 transplant recipients (25 lung, 22 other solid organs, 13 bone marrow). Clinical charts were reviewed.

Results and conclusions: EBV was detected in 29/108 (26.8%) specimens from 23/60 (38.3%) patients: 17/68 (25%) from 12/25 (48%) lung transplant recipients; 8/23 (34.8%) from 8/22 (36.4%) other solid organ transplant recipients, and 4/17 (23.5%) from 3/13 (23.1%) bone marrow transplant recipients. Prevalence of EBV did not significantly differ between lung transplant patients and other solid organ and/or bone marrow transplant recipients. Viral load was significantly lower in lung transplant vs all the other transplants (250.5 ± 454.2 copies/ml BAL vs 2967 ± 4649 ; $p=0.023$) and in lung transplant patients vs other solid organ transplant recipients (250.5 ± 454.2 vs 4345 ± 5447 ; $p=0.004$). In lung transplant patients EBV (at low viral load) was frequently detected during routine follow-up bronchoscopies in the absence of clinical and/or radiological signs or symptoms, while in other transplant patients EBV was detected (at viral load $>10^4$) in the presence of pneumonia or respiratory insufficiency. These results suggest that although EBV positivity is frequent in lung transplant, as well as in other transplants, the clinical impact of EBV in this group of patients could be lower. The possible role of CMV combined prophylaxis (CMV-Ig + ganciclovir or valganciclovir) in lung transplant patients needs further studies, aimed to elucidate also the potential underlying biological mechanism.

CLINICAL EPIDEMIOLOGY OF HUMAN CYTOMEGALOVIRUS IN LUNG TRANSPLANT RECIPIENTS

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Rationale and aims: HCMV is a major pathogen in transplant recipients. As the lung is a latency site of HCMV, its detection in bronchoalveolar lavage (BAL) from lung transplant patients should be interpreted taking into account the clinical context and viral load. The aim of this study was to investigate the clinical epidemiology of HCMV in lung transplant vs other solid organ transplant recipients.

Methods. 91 BAL specimens from 26 lung transplant recipients (sampling schedule: at month 1 post-transplantation, then at 3-month intervals) and 31 from as many other solid organ transplant recipients (liver 13, kidney 11, heart 7) were evaluated for HCMV by rapid shell vial culture and Real Time TaqMan PCR. Discharge diagnosis according to the ICD9CM classification was recorded.

Results and conclusions. HCMV resulted positive in 32/91 (35.2%) specimens from 15/26 (57.7%) lung transplant patients vs 10/31 (32.2%) in other solid organ transplant recipients (p=n.s.). In lung transplant patients, HCMV was found both in the absence (follow-up sampling) and in the presence of clinical and/or radiological signs or symptoms, including transplant complications, respiratory insufficiency, and other pneumopathies. In particular, a diagnosis of pneumonia was made in 13/32 (40.6%) samples from 5/15 (33.3%) patients, all of them with a viral load $>10^5$ copies/ml BAL. In other solid organ transplant recipients, a diagnosis of pneumonia was made in 6 HCMV-positive patients, however viral load was $>10^5$ only in one kidney transplant recipient. Our results confirm the relevant role of HCMV as pathogen responsible of pneumonia in transplant recipients; viral load tended to be higher in lung transplant recipients, thus suggesting that an impaired pulmonary background may favour viral replication.

RISK MANAGEMENT OFFICE, INFECTION CONTROL COMMITTEE AND MEDICAL DIRECTION: WHICH IS THE BEST WAY FORWARD TO CONTROL HEALTHCARE-ASSOCIATED INFECTIONS?

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Healthcare-associated infections (HAI) control and prevention have a long-time history as clinical risk orderly managed by Health Care Organizations (HCO).

In the '80 the SENIC study stood out that the practical engagement of the HCO can produce a significant HAI reduction. After those results guidelines were universally produced and spread (in Italy the Ministry of Health Recommendations n. 52/85 and 8/88) and even today HCOs should refer to them. The concept of a multidisciplinary committee (Infection Control Committee [ICC]), the involvement of the medical direction as warrantor and promoter of the program throughout the organization, the presence of Infection Control Practitioners (ICP) and programs for surveillance and control are fundamental tools that must be in place in every HCO to effectively control HAI. In the '90 some further developments enriched the management of HAI prevention.

The first one is the approach to quality in health care and the consequent adoption of specific indicators. HAIs are universally recognised as a good indicator of healthcare quality and most of the accreditation systems include specific standards on this. Those HCOs that want a recognition of their efforts in quality improvement, should demonstrate their skills on prevention and control of HAI risk too (1).

The second fact is that actions driven by the macro-systems level can produce a significant improvement on HAIs control. In Italy the concept of macro-system refers both to Regional and National government and a key element is the Coordination between State and Regions; in other countries as U.K. (England, Scotland, etc.), France, Sweden the national level is prevalent.

Actions at the macro-system level deal with mandatory report of specific events (i.e. multi drug resistant (MDR) micro organisms, surgical site infections, etc.), economic resources constrained to the achievement of specific performances by organizations, managers and professionals, etc..

As macro-system actors the European Union recently produced recommendations about clinical risk and HAI risk in HCO, the European Centre for Disease Prevention and Control (ECDC) dedicated a team to coordinate the members-state policies and the World Health Organization (WHO) promoted the World Alliance for Patient Safety program (2, 3).

The third fact is the attention about clinical risk and its organizational, professional, legal and insurance implications.

The approach to HAI is similar to clinical risk and it can be considered an important

part of this last one. But HAI control programs still maintain its autonomy because of the risk frequency, the specific knowledge and the needed specific training for professional profiles. HAIs have a relevant impact on legal and insurance instances too: HCOs need to warrantee good insurance contracts and reduce insurance premium.

The fourth fact is the central role of patients with respect to performance evaluation and to clinical pathways definition. Media and citizen attention is increasing about how healthcare organizations and workers perform and about adverse events that can occur.

Some years ago SIMPIOS (Italian Multidisciplinary Society for Health Care Associated Infections in Health Care Organizations) produced some recommendations to promote HAI risk control culture and programs in Italy.

In the document was reported that the following elements are fundamental: to share programs with all HCO workers, the presence of a dedicated operative group, the presence of at least one ICP for every HCO (better one for two hospitals than one not dedicated); the availability of medical skills (epidemiology, hospital hygiene, pharmacy, infectious diseases, microbiology, etc.); availability of “ad hoc” work place, equipment, bibliographical documentation, internet connections, microbiologic services and referral network; surveillance on infections, sentinel micro-organisms, antibiotic resistance; presence of guidelines, procedures and policies, properly produced, spread with appropriated methodology, checked for the implementation, periodically revised; specific training on problem solving, communication, leadership and management.

Nowadays to those recommendations we should add that (4, 5):

- it is necessary a leading action at macro levels (regional, national governments, etc.);
- the involvement of HCO general manager and particularly of the medical director is essential but it plays an important role also the “collegio di direzione”, a collegial healthcare organization’s advising body;
- it must be put in place a qualified working team, that can be also shared among organizations, focused on the topic and with the mission and capability to effectively and concretely intervene. This team must include the ICP;
- policies and actions for clinical and HAI risks should be integrated even if the infectious risk needs to maintain its specificity;
- to translate scientific evidence into daily practice is the actual challenge and the performance monitoring is an essential element;
- to modify and enrich professional knowledge, attitudes and practice is necessary to promote the baseline and continuous educational training; a appropriated management both of clinical and HAI risks should be considered an essential part of the professional activity.

We know that there’s no a better way to control HAIs risk but we need to model effectively in each single situation the existing evidences with the organization’s history, the professional and organizational culture as well as the professionals and their behaviours.

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