An active microbiological surveillance project at an Italian teaching Hospital: microbial isolates, recent epidemiological trends, major clinical concerns, and antimicrobial susceptibility rates during a four-year period

Un progetto di sorveglianza microbiologica attiva in un Policlinico Universitario Italiano. Ceppi microbici isolati, recente andamento epidemiologico, principali ricadute cliniche, ed indici di antibiotico-sensibilità in un arco di tempo di quattro anni

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INTRODUCTION

Novel epidemiological changes and resistance problems have emerged recently, especially among hospital pathogens like staphylococci, enterococci, Pseudomonas spp., and other Gram negative rods. Whereas novel molecules have been and are being developed for treating Gram positive infections, difficult pandrug-resistant Gram negative infections are expected to become an increasing therapeutic challenge in the next future [1-5]. Routine hospital (and possibly community) surveillance programs are critical for creating and refining approaching to controlling antimicrobial resistance, and for guiding clinical decisions on the pathway of appropriate drug choices. Longitudinal studies are particularly useful since relevant information can be obtained by comparing data over time. In our case, an active, prospective microbiological surveillance of all bacterial and fungal microorganisms isolated from inpatients at a tertiary care reference hospital, and their in vitro antimicrobial susceptibility trends, in our opinion is of paramount importance in building awareness of evolving local epidemiology, and in planning effective preventive and therapeutic strategies [3, 4, 6]. Moreover, the knowledge of the clinical and economic impact of multiresistant infections and antimicrobial resistance is extremely useful to influence programs and behaviour in health care facilities, to guide policy makers and funding institutions in the light of length of hospital stay, adverse events, and increased expenditures, to define the outcome of individual patients, and to stimulate interest in a correct use and especially in the research and development of new antiinfective agents [2-5, 7].

PATIENTS AND METHODS

An active bacteriological- mycological surveillance project has been judged mandatory as a part of the necessary basic knowledge on the local microbial isolation, and the local microorganism and antibiotic resistance maps, at our Hospital (S. Orsola-Malpighi General Hospital, Bologna, Italy). Complete figures and trends of microbial (bacterial and fungal) isolations from all hospitalized patients are consistently registered in a
standardized software, and are periodically reported to all health care providers on quarterly basis, together with results of the *in vitro* antimicrobial sensitivity testing, compared with those of previous months and years [8].

For the present report, a four-year period (ranging from January 1, 2004, up to December 31, 2007), has been comprehensively assessed to observe eventual epidemiological trends, to focus several emerging clinical problems, and to evaluate the parallel trend of antimicrobial sensitivity assays systematically performed on the isolated organisms.

Some clinical and microbiological topics (i.e. central vascular catheter infections, urinary tract infections, *in vitro* susceptibility of emerging microorganisms like enterococci and *Pseudomonas aeruginosa*, as well as the phenomenon of extended spectrum beta-lactamase (ESBL) production, have been analyzed in depth, on the ground of the updated data of the last available year of observation (year 2007).

Commercial, standardized laboratory techniques were consistently used during the entire study period, in order to obtain microbial growth and reliable identification, and to assess the *in vitro* antimicrobial susceptibility rates according to the updated international reference standards [8].

From a methodological point of view, all surveillance cultures were ruled out from the present study, while multiple isolations of the same organism(s) obtained from one single patient within one month of hospitalization, accounted for one isolation only (i.e., they have been considered only once), in order to reduce isolation biases, and their subsequent microbiological and antimicrobial susceptibility analysis, performed on overall basis.

From a statistical point of view, continuous variables were assessed through Student *t* test, while Mantel-Haenszel chi-square test (or Fisher exact test), were adopted to evaluate non-continuous variables. Statistical significance has been posed at *p* values <0.05, as usual.

## RESULTS

### Overall microbiological survey from the entire observation period (years 2004-2007)

The temporal trend of microbial isolates from patients admitted during the last four calendar years (2004 to 2007), has been assessed according to the main bacterial and fungal cultures obtained from inpatients, as specified above. On the whole, the main pathogen group remained that of Enterobacteriaceae (6,608 isolations out of 19,666 overall strains, equivalent to 33.6%, with *Escherichia coli* retrieved in 60-75% of cases), without significant differences noticed over the four-year observation time. Staphylococci (4,150 isolates), and enterococci (3,276 isolates), proved the two largest groups after Enterobacteriaceae, but staphylococci significantly declined in their frequency during the examined four-year period (from 23.8% to 16.2%; *p*<0.001), mainly due to a reduced isolation of coagulase-negative staphylococci (possibly attributable to a reduced rate of contaminated blood cultures). In the same time, a slight increase of enterococci occurred (from 15.4% of year 2004 to 18.6% of year 2007; *p*<0.05). Based on the frequency of isolation, Gram negative oxidase-positive organisms accounted for 2,109 episodes, followed by other aerobe Gram positive organisms other than staphylococci-enterococci (613 isolates), and anaerobe organisms (583 isolates): no significant temporal variations occurred over time for these last microbial groups. With regard to Gram negative oxidase-negative microorganisms (567 isolates), non-beta-haemolytic streptococci (464 cases), and beta-haemolytic streptococci (260 isolates), a significant trend towards a reduction of frequency occurred from the year 2004 to 2007 (*p*<0.05 to *p*<0.001). Finally, fungal infections accounted for 1,036 overall episodes, in over 80% of cases represented by the yeast *Candida* spp.

### Year 2007: an updated microbiological perspective

On the whole, 5,256 overall valuable pathogens were cultured and identified in the last 12 valuable months (January 1, up to December 31, 2007), with *E. coli* (1,144 strains), *Enterococcus faecalis* (697), *P. aeruginosa* (439), and *Staphylococcus aureus* (389) being the prevailing organisms. Among blood cultures (1,035 overall isolates), a major role was played by staphylococci as a group (328), followed by enterobacteriaceae (222), and enterococci (114).

With regard to the overall susceptibility rates, methicillin-resistant *S. aureus* accounted for a mean 46.5% rate, while methicillin resistance was greater for *S. epidermidis* (83.5%); anyway, no significant changes were found during the examined time. Substantially unchanged *in vitro* sensitivity levels were found among enterococci, with only four “Van-A” *E. faecalis* strains,
and 14 “Van-B” Enterococcus faecium strains recorded: a slight increase of resistance towards glycopeptides was therefore found, reaching nearly 3% of isolates, concentrated in the last three months of the year 2007.

A 26-40% resistance rate to macrolides was found among streptococci, without appreciable temporal variations. Among Gram negative organisms, the ESBL production regarded 23.5% of E. coli isolates, and 38.3% of other Enterobacteriaceae, again without a significant increase during time. P. aeruginosa showed an increased antibiotic resistance trend towards penicillins and cephalosporins (including those protected by beta-lactamase inhibitors), carbapenems, fluoroquinolones, and aminoglycosides (60-80% of strains), but remained full susceptible to colistin. Stenotrophomonas maltophilia confirmed its extensive resistance spectrum, but remained 90-100% sensitive to cotrimoxazole and colistin, as well as Acinetobacter spp., which showed a favourable susceptibility rate (60-100%) to aminoglycosides, piperacillin-tazobactam, and colistin.

Focus on sepsis-bacteraemia: microorganisms isolated from blood cultures (entire 2004-2007 period)

Of 4,606 overall episodes of hospital-diagnosed sepsis-bacteraemia, Staphylococcus epidermidis remained the leading organism (983 cases: 21.3%), but a dramatic drop in its frequency occurred during the observation time (from 26.1% of overall episodes in the year 2004, to only 14.3% in the year 2007; p<.001). The second aetiological agent of bacteraemia was represented by E. coli (463 episodes: 10.1%), followed by S. aureus (327 cases: 7.1%), E. faecalis (245 episodes: 5.3%), P. aeruginosa (170 cases: 3.7%), Klebsiella spp. (123 episodes: 2.7%), and E. faecium (117 cases: 2.5%). Significant time-based modifications occurred only for P. aeruginosa (temporal increase: p<.02), Klebsiella spp. (temporal increase: p<.001), and E. faecium (temporal increase: p<.05). Among fungi, Candida albicans was the most represented organism, with 104 episodes (2.3%), without changes in its frequency in the examined 2004-2007 period.

Focus on urinary tract infections among hospitalized patients (an analysis of nearly 2,400 episodes registered in the year 2007)

The temporal trend of microbial isolates from urines of inpatients hospitalized during the last calendar year (2007), was evaluated quarterly according to the main bacterial and fungal isolates. Of 2,384 overall episodes (as defined above), 920 (38.6%) were determined by E. coli, followed by E. faecalis (541 episodes: 22.7%), P. aeruginosa (140 cases: 5.9%), Klebsiella spp. (134 episodes: 5.6%), Proteus mirabilis (118 cases: 4.9%), E. faecium (76 episodes: 3.2%), while the first fungal pathogen was again Candida albicans (87 episodes: 3.6%). During the proportionally short (one-year) observation period, no significant variations occurred in the frequency of isolation of each mentioned urinary tract pathogen, when excluding a mild increased frequency of E. faecium during time (p<.05).

A four-year trend of in vitro sensitivity profile of Staphylococcus aureus strains

The progressively increased rate of drug resistance among Gram positive cocci is a general concern, especially in hospital settings. The temporal variations of the in vitro antimicrobial sensitivity figures were examined quarterly for all suitable S. aureus strains, and followed from year 2004 to year 2007. Among overall S. aureus isolates (1,863 strains tested on the whole), a complete (100%) sensi-
tivity was shown against both glycopeptide antibiotics vancomycin and teicoplanin, while some compounds retained interesting activity (92.0% to 97.1% for cotrimoxazole, 76.1% to 88.7% for chloramphenicol, 64.1% to 69.5% for rifampin). Oxacillin (methylcillin) resistance ranged from a minimum mean rate of 46.2% (year 2007), to a maximum mean rate of 53.3%, registered during the year 2005. As a consequence, beta-lactam derivatives proved an in vitro activity ranging from 46.7% to 54.1% for co-amoxiclav, 46.6% to 54.1% for cefotaxime, and only 7.3% to 11.2% for penicillin. Among other tested molecules, clindamycin reached a comprehensive ~50% susceptibility rate (40.8% to 54.3% of all tested strains), followed by erythromycin (40.3% to 54.7%), and gentamicin (42.6% to 49.5%). As a consequence, no statistically significant temporal variations of antimicrobial susceptibility rates occurred during the four-year study time.

**In vitro antimicrobial susceptibility trends of Enterococci (years 2004-2007)**

The temporal trend of the in vitro antibiotic susceptibility rates was examined for all *E. faecalis* and *E. faecium* strains, isolated at our General Teaching Hospital during the years 2004-2007. Among *E. faecalis* isolates (2,736 strains tested on the whole), the greater activity rate was achieved by linezolid (100% of tested strains), followed by teicoplanin (97.9% to 100% of tested strains), nitrofurantoin (96.4% to 98.3% of isolates), vancomycin (81.0% to 100%), ampicillin (90.2% to 91.9%), penicillin (88.8% to 91.5%), while irregular variations of sensitivity occurred over time for gentamicin (above 60% of tested strains), streptomycin (above 70% of overall strains), and tetracyclines (less than 20% of tested strains). When considering *E. faecium* strains (626 overall isolates), only linezolid maintained a 100% in vitro activity, followed by teicoplanin (87.7% to 100% of tested strains), vancomycin (78.4% to 86.2% of isolates), tetracyclines (56.8% to 81%), and gentamicin (59.1% to 71.0%), while an unpredictable in vitro efficacy was shown by streptomycin (27.6% to 69.8% of tested strains). A globally increased in vitro resistance rate was also detected for tetracyclines, during the entire four-year study period (*p*<.01). Sixty-six overall strains of vancomycin-resistant enterococcal (VRE) strains were detected, with a clearly increased trend from the year 2004 (7 cases only), up to the year 2007 (21 cases) (*p*<.001).

**Enterococci cultured in the year 2007: an update on isolated strains and their trend of antimicrobial susceptibility features**

*In vitro* antibiotic susceptibility rates were prospectively investigated for all *E. faecalis* and *E. faecium* strains, isolated at our tertiary-care hospital during the year 2007, which have been reported every three month in order to monitor their epidemiological, clinical, and therapeutic concerns.

Among *E. faecalis* isolates (705 strains tested on the whole), the greater antibiotic activity rate was achieved by linezolid (100% of tested strains), followed by nitrofurantoin (97.4% to 100% of isolates), teicoplanin (94.8% to 100%), vancomycin (87.5% to 100%), ampicillin (89.0% to 92.4%), penicillin (87.9% to 91.0%), while appreciable, but irregular variations of sensitivity occurred over time for gentamicin, streptomycin, and tetracyclines.

With regard to *E. faecium* strains (175 strains), both linezolid and teicoplanin maintained a 100% in vitro activity, followed by vancomycin (86.4% to 100% of strains), streptomycin (62.5% to 100% of isolates), gentamicin (52.9% to 63.6%), and tetracyclines (51.8% to 49.6%), while negligible efficacy was shown by ampicillin (7.5% to 18.5% of tested strains), and penicillin (7.5% to 18.5%).

Eighteen strains of vancomycin-resistant *E. faecalis* strains were detected (12 concentrated in the July-September period), while vancomycin-resistant *E. faecium* strains were six through the entire observation year (2007).

No significant temporal modifications of antimicrobial sensitivity rates were observed, as well as no significant change in the emergence of vancomycin-resistant strains during time.

**Escherichia coli and other Enterobacteriaceae. In vitro antimicrobial susceptibility trends (years 2004-2007)**

The continued modification of drug resistance rates among Enterobacteriaceae is a relevant issue, especially in hospital facilities. The temporal variations of the in vitro antimicrobial sensitivity trends were updated quarterly for all suitable Enterobacteriaceae strains, followed from January 1, 2004, up to December 31, 2007. Among overall *E. coli* isolates (4,413 strains tested on the whole), imipenem and colistin maintained a full (100%) in vitro activity, followed by amikacin (97.3% to 99.5% of tested strains), nitrofurantoin (89.2% to 94.8%), pipercillin-tazobactam (89.0% to 93-9%), gentamicin
(81.9% to 89.4%), ceftazidime (78.3% to 89.5%), cefotaxime (78.0% to 89.8%), and ciprofloxacin (63.8% to 73.9%). When considering Enterobacteriaceae other than E. coli, imipenem and colistin remained 100% active, followed by amikacin (94.9% to 97.2% of tested strains), piperacillin-tazobactam (78.4% to 86.0%), ceftriaxone (72.1% to 78.0%), gentamicin (74.0% to 77.3%), norfloxacin (66.4% to 76.2%), cefazidime (62.7% to 69.7%), and cefotaxime (62.3% to 69.0%). The emerging spread of ESBL production among this microbial pathogens significantly reduced the activity of third-generation cephalosporins over time (from a mean of 89.7% of susceptible E. coli strains in the year 2004, to 78.1% in the year 2007; p<.001; and from a mean of 69.7% of sensitive Enterobacteriaceae strains in the year 2004, to 62.4% in the year 2007; p<.03).

Also fluoroquinolones and beta-lactam molecules protected by suicide beta-lactam inhibitors suffered from a drop of their in vitro sensitivity rates (p<.02 to p<.005).

**Pseudomonas aeruginosa: antimicrobial susceptibility trends over a four-year observation period (2004-2007)**

Particular attention has been deserved to *P. aeruginosa*, as a leading Gram negative organism, which often tests multiresistant especially among inpatients and in hospital settings. The temporal variations of the in vitro antimicrobial sensitivity rates of all isolated *P. aeruginosa* strains were collected for all suitable isolates, during the four-year period ranging from January 2004, up to December 2007.

Among overall *P. aeruginosa* isolates (2,083 valuable tested strains), the best performance was obtained by the old colistin (colimycin), with a sustained 100% in vitro susceptibility rate, followed by amikacin (72.8% to 81.2% of tested strains), imipenem (76.8% to 80.8%), piperacillin-tazobactam (70.9% to 78.7%), cefazidime (68.9% to 77.1%), and tobramycin (64.6% to 70.9%).

On the other hand, gentamicin (55.1% to 63.5% of tested strains), aztreonam (57.5% to 66.8%), ciprofloxacin (55.7% to 65.0%), ticarcillin-clavulanate (53.7% to 60.5%), and mezlocillin (48.4% to 55.2%), proved less affordable in their antimicrobial susceptibility patterns, significant changes were observed only for ceftazidime and ciprofloxacin (p<.03) (with their drop of susceptibility, essentially due to the frequent production of ESBL by microbial strains).

**The effect of microbial extended-spectrum beta-lactamase production on antibiotic susceptibility figures, in the year 2007**

The increased rate of antimicrobial resistance among Gram negative rods and all Enterobacteriaceae as a whole is a major concern, especially in the hospital setting.

The prospective microbiological surveillance of antimicrobial susceptibility rates ongoing at our Hospital, has been implemented during the year 2007 with an analysis of the relationship with the emergence of ESBL production. Among *E. coli* isolates (493 strains tested on the whole), imipenem proved in vitro effective in 100% of cases, followed by piperacillin-tazobactam (86.6% to 90.6% of tested strains), nitrofurantoin (86.1% to 91.7% of strains), ceftazidime (75.8% to 79.8%), cefotaxime (75.7% to 79.8%),...
co-amoxiclav (61.7% to 69.8%), ciprofloxacin (61.0% to 64.3%), and norfloxacin (64.5% to 70.2%). Both cefotaxime and ceftazidime sensitivity (seriously affected by the production of ESBL), showed a drop from a 79.8% mean susceptibility rate observed during the first quarter of year 2007, to a mean 75.7% of the last quarter of the same year 2007.

With regard to Enterobacteriaceae as a whole (other than \textit{E. coli}), among 753 comprehensive isolates, both imipenem and colistin retained full (100%) \textit{in vitro} activity, followed by piperacillin-tazobactam (72.5% to 81.5% of tested strains), cotrimoxazole (71.6% to 77.6%), gentamicin (71.6% to 76.1%), ciprofloxacin (64.1% to 68.6%), ceftazidime (60.8% to 64.5%), norfloxacin (60.2% to 69.8%), and cefotaxime (59.7% to 62.7%), with cephalosporins moderately affected by ESBL production, although in absence of significant temporal modifications.

**DISCUSSION**

An active, prospective bacteriological-mycological surveillance project may notably add to the knowledge of local epidemiological figures and \textit{in vitro} antimicrobial sensitivity trends, therefore playing a major role when planning surveillance measures, chemoprophylaxis regimens, and empiric antimicrobial treatment, especially on local and regional basis [2-4, 7, 9-12], among both adult and paediatric patients [13]. A prospective microbiological monitoring with periodic reports (quarterly web-accessible and hospital-shared reports in our case), is expected to significantly contribute in the selection of both chemoprophylaxis and treatment choices of antimicrobial compounds, contributing to contain the spread of microbial resistance among inpatients, indirectly in the hospital environment, and secondarily in the community. Although Enterobacteriaceae remain the major causative agents of inpatient infections, a significant decline of coagulase-negative staphylococci, all streptococci, and \textit{Gram} negative oxidase-negative organisms occurred over the examined four-year period, while enterococci showed a mild increase over time in our experience. Special attention should be deserved to bacteraemias and sepsis, which are responsible for considerable morbidity and mortality rates among inpatients [6, 7, 11, 13]. Although the main etiological agents of inpatient bacteraemias are still represented by coagulase-negative staphylococci, these microorganisms significantly declined in their overall figures during our four-year study period, thus confirming a positive trend towards a progressively reduced incidence of contaminated blood cultures. On the other hand, an appreciable increased frequency occurred over time for \textit{Pseudomonas}, \textit{Klebsiella}, and \textit{Enterococcus} spp., as already noticed [6, 13]. A major, persisting role as an agent of hospital bacteraemic episodes was still exerted by \textit{E. coli} among \textit{Gram} negative pathogens, and by \textit{S. aureus} among \textit{Gram} positive ones. Central vascular catheter (CVC) infections represent relevant causes of hospital-related morbidity and mortality, and their careful monitoring plays a highly significant role in the selection and planning of chemoprophylactic and therapeutic choices in high-risk settings like surgical and intensive care units, on both local and regional settings [6, 14, 15]. Although the major causative agents of CVC-related infection among hospitalized patients remain staphylococci as a group (as already known), however the progressive emerging of \textit{Gram} negative pathogens is appreciable also over a proportionally short (12-month) observation period, and deserves major attention by microbiologists and clinicians involved in clinical care with specific competences [6, 14, 15]. On the other hand, urinary tract infections are responsible for considerable morbidity among a large number of inpatients, burdened by multiple risk factors for these infections, some of them deserving accurate monitoring and selection of appropriate devices [10, 16-18].

During the still limited observation time of our study, modest variations occurred in the frequency of isolation of the most frequent microorganisms, with \textit{E. coli} representing nearly 40% of cultured organisms, followed by \textit{E. faecalis} (which proved responsible of around 23% of overall episodes).

The tendency towards an increased incidence of \textit{E. faecium} as an agent of urinary tract disease is of great concern, given the unpredictable antibiotic sensitivity profile of this last emerging \textit{Gram} positive microorganism [18]. When considering the microbiological perspective, seen through the main microbial pathogens, \textit{S. aureus} seems to play a steady, significant role among inpatients, due to its frequency, pathogenicity, broad range of clinical features, and elevated frequency of antimicrobial resistance rates [19]. Methicillin resistance
is a well known marker of a wide range of antimicrobial resistance in these organisms, so that it is carefully monitored through countries and with supranational projects [6, 7, 9, 19].

In our experience, despite a stable, significant rate of methicillin resistance rate (mean value around 47% of all S. aureus isolates in a four-year period), we have to underline that “older” antimicrobial compounds like cotrimoxazole, chloramphenicol, and also rifampin, may still play some role in selected clinical situations (possibly as add-on agents), while the activity of both available glycopeptides was completely preserved in our experience [20].

With regard to enterococci as a group, the emerging in vitro resistance to some reference compounds, and the initial record of some sparse vancomycin-resistant strains in particular, may be adequately monitored on temporal basis as planned by our study, in order to address the clinical choices according to the local epidemiology and antimicrobial testing features. The emerging of in vitro resistance to some reference compounds like glycopeptides may be also well targeted on these basis, in order to preserve the clinical use of the majority of molecules which still guarantee effective activity of these difficult-to-treat Gram positive cocci (i.e. novel agents with extended activity against multiresistant Gram positive cocci, like linezolid, quinupristin-dalfopristin, dalbavancin, oritavancin, telavancin, ceftobiprole, and ceftaroline) [21].

When considering E. coli and the vast spectrum of Enterobacteriaceae, despite a maintained activity of all carbapenems and that of the old colistin, a significant trend towards increased antimicrobial resistance rates was found over a four-year observation period, with ESBL secretion playing a major role in their resistance pathways, as already shown [1, 12, 17, 22-24].

A prospective monitoring of antimicrobial susceptibility rates of a major hospital-associated and environmental organism like P. aeruginosa is relevant, to add to local and national guidelines of antibiotic treatment and prophylaxis [7, 25]. Despite a progressive, significant increase of resistance rates against the majority of compounds which usually test active against P. aeruginosa, amikacin, carbapenems, piperacillin-tazobactam, amikacin, and ceftazidime still maintain a reliable role in eventual, empiric regimens to be added pending microbial isolation and in vitro susceptibility studies, since they remained active in nearly 80% of hospital isolates during the last study year (2007). Finally, the increased rate of in vitro antimicrobial resistance among Gram negative rods and all Enterobacteriaceae as a whole represents a major concern, especially in the hospital setting and among compromised inpatients. An analysis of the relationship with the emergence of ESBL secretion also confirmed the major role of this last mechanism in the spread of resistance determinants [1, 22-24, 26].

Prospective surveillance studies of the in vitro antimicrobial sensitivity rates of some relevant hospital-associated organisms like E. coli and Enterobacteriaceae are an useful guidance to plan cost-effective antibiotic treatment and prophylaxis, on local and regional basis, also taking into account the environmental perspectives of antibiotic usage [4, 6, 7, 22-26].

These last Gram negative groups also allow a reliable study of the temporal trend of ESBL production, since this feature significantly affects the activity of multiple broad-spectrum antimicrobial compounds against these commonly isolated Gram negative microorganisms. Among them, an increasing concern is focused on organisms like Acinetobacter spp., which test resistant to almost all antimicrobials directed against Gram negative rods, and often require an association of the old colistin with carbapenems, tigecycline, rifampicin, or other agents carefully selected on the ground of extended in vitro sensitivity testing [27, 28].

The reported data and their continued update and discussion on the basis of the most recent literature evidence, underline the importance of well-constructed epidemiological studies to determine the prevalence of antimicrobial resistance in daily clinical practice, and the central
place of reference laboratory-based in vitro sensitivity testing in predicting antimicrobial chemotherapy and subsequently in optimizing patient outcomes. As health care systems vary widely, planning and prevention strategies must be designed accordingly, although economics in general, cost factors, and resource planning are becoming common issues to almost all countries.

Key words: microbiological surveillance, epidemiology, antimicrobial susceptibility.

A microbiological surveillance program is currently performed at our tertiary-care teaching hospital. The temporal trend of microbial isolates from patients admitted during four calendar years (2004 to 2007) was analyzed according to the main bacterial and fungal culture organisms. The same pathogens isolated more than once from the same patient within one month were considered only once.

On the whole, the main pathogen group remained that of Enterobacteriaceae (6,608 isolations out of 19,666: 33.6%, with Escherichia coli found in 60-75% of cases), with no significant difference over time. Staphylococci (4,150 isolates), and enterococci (3,276 isolates) were the two largest groups after Enterobacteriaceae, but staphylococci significantly declined during the four-year period (p<.001), mainly due to progressively reduced isolation of coagulase-negative staphylococci.

By contrast, a slight increase in enterococci occurred (p<.05).

Based on the frequency of isolation, Gram-negative oxidase-positive organisms accounted for 2,109 episodes, followed by other aerobic Gram-positive organisms other than Staphylococci-Enterococci (613 isolates), and anaerobes (583 isolates): no significant variations occurred over time for these last microbial groups.

With regard to Gram-negative oxidase-negative microorganisms (567 isolates), non-beta-haemolytic streptococci (464 cases) and beta-haemolytic streptococci (260 isolates), a significant reduction of frequency occurred from 2004 to 2007 (p<.05 to p<.001).

Finally, fungal infections accounted for 1,036 overall episodes, in over 80% of cases represented by Candida spp.

Prospective microbiological monitoring is expected to contribute significantly to our knowledge of local epidemiological figures and antimicrobial sensitivity profile of hospital infections, and plays a major role in selecting both treatment and chemoprophylaxis schedules, especially on a local-regional basis.

Although the major causative agents of in-patient infections remain Enterobacteriaceae, a significant decline in coagulase-negative Staphylococci, all Streptococci, and Gram-negative oxidase-negative organisms occurred over the four-year period, while Enterococci showed a mild increase over time.

**SUMMARY**

Presso il nostro Policlinico Universitario è in corso un programma di sorveglianza microbiologica attiva. Abbiamo esaminato l’andamento nel tempo dei microrganismi isolati da pazienti ospedalizzati nel corso degli ultimi quattro anni (2004-2007), a seconda delle principali specie batteriche e fungine identificate. Gli stessi agenti patogeni isolati più di una volta dal medesimo paziente nell’arco di un anno, sono stati considerati come un solo eziologico. Nel complesso, la maggior parte degli isolati apparteneva al gruppo delle Enterobacteriaceae (6,608 isolati su 19,666: 33.6%, con Escherichia coli responsabile nel 60-75% dei casi), in assenza di significative modificazioni temporali. Gli stafilococchi (4,150 isolati), e gli enterococci (3,276 ceppi), rappresentavano i due gruppi più numerosi dopo le Enterobacteriaceae, ma nell’arco dei quattro anni di studio si assisteva ad una significativa riduzione degli stafilococchi (p<.001), da ascrivere per lo più ad una progressiva riduzione del rilievo di stafilococchi coagulasi-negativi. Nel contempo, si registrava invece un lieve incremento dell’isolamento di enterococchi (p<.05). Sulla base della frequenza di rilievo in coltura, i microrganismi Gram negativi, ossidasi-positivi, erano responsabili di 2,109 episodi, seguiti da batteri aerobi Gram positivi diversi da stafilococchi ed enterococchi (613 isolati), e da batteri anaerobi (583 isolati), in assenza di significative variazioni temporali. Per quanto attiene ai germi Gram negativi, ossidasi-negativi (567 isolati), agli streptococchi non-beta-emolitici (464 casi), e agli streptococchi beta-emolitici (260 isolati), si osservava una tendenza verso una significativa riduzione di frequenza dall’anno 2004 al 2007 (da p<.05 a

**RIASSUNTO**
REFERENCES


