Microbiological sentinel events at a neurological hospital: a retrospective cohort study

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The purpose of this study is to describe the epidemiological surveillance of microbiological sentinel events (SEs) carried out between 2012 and 2014 at the Neurological Hospital Carlo Besta, Milano, Italy. The setting is inpatient care with multidrug-resistant infections. The aim of the procedure is to formalize the management mode, reporting and transmission of SEs.

The incidence rates of SE were calculated per 1000 patient-days and for 100 admissions using Poisson distribution. The incidence rate of isolation for 1000 patient-days varies from a minimum of 0.52 (95% confidence interval, 0.23–1.15) for the second quarter of 2014 to a maximum value of 4.16 (95% confidence interval, 3.20–5.40) for the first quarter of 2013. A decrease followed from the third quarter of 2013 that remained constant in 2014, reaching values similar to those of 2012. Preventive actions and their effectiveness on Acinetobacter baumannii, the primary cause in our division of multidrug-resistant infections in 2012, have ensured a reduction of the incidence of the same; preventive actions and their effectiveness allowed us to intercept microbiological SE and trigger appropriate precautionary behaviour and isolation. Surveillance of healthcare-associated infections is fundamental in understanding the sources that are contributing to the growing reservoir within hospital communities.

INTRODUCTION

One of the most obvious problems concerning healthcare-associated infections (HAIs) is the detection of microbiological sentinel events (SE). By SEs, we mean the individual first investigations of micro-organisms that are included in a hospital surveillance programme for their particular antibiotic resistance; the symptoms of the disease may appear or not, while the individual concerned is hospitalized. One of the strategies, known as health surveillance of infectious diseases in a precise population, is monitoring microbiologically positive results to survey the presence of microbial agents known to be dangerous to health (Zeng et al., 2011).

SE indicate the presence of inadequate working conditions and the exposure to unacceptable risk factors such as the utilization of medical procedures, high-risk medical interventions and invasive devices, and failure of the hospital’s efforts to prevent infections that require an individual investigation (Emori & Gaynes, 1993; Kluytmans–VandenBergh et al., 2005). HAIs (Vincent, 2003) that develop 48 h after hospital admission of the patient (Custovic et al., 2014) are dependent on two key pathophysiological factors: decreased host defences and colonization by pathogenic organisms; and infected or colonized patients who frequently serve as reservoirs of bacterial infection for other patients (Jarvis, 1996). It has been demonstrated that each night spent in hospital increases, by 5%, the risk of acquiring hospital infections (Hauck & Zhao, 2011), and prolonged patient-days necessitate a number of medical procedures that increase the possibility of transferring hospital infectious pathogens (Hauck & Zhao, 2011; World Health Organization, 2002). Not all SE related to extrinsic risk factors (patient care staff must not forget the critical role of hand washing in preventing the transmission of SE) are preventable, since the benefits of the continued use of invasive devices, such as urinary catheters and central venous and arterial catheters, compromises normal skin and mucosal barriers, predisposing them to infection.
The duration of catheterization is a very important risk factor for developing infection (Lo et al., 2014; Ronzani et al., 2013), and inappropriate treatment of catheter-associated asymptomatic bacteriuria promotes antimicrobial resistance and Clostridium difficile infection (Johnson et al., 1990). For an effective defence against HAI, criteria identification and monitoring must be homogeneous; that is to say that the definitions, description of appearance circumstances, methods of analysis and monitoring should be codified and commonly understood.

The sources of information available to the hospital to detect infected patients, such as microbiology laboratories, have a crucial role in early identification of SE and in detecting trends of antibiotic resistance (Cope et al., 2009). The most widely disseminated and accepted guidelines are those developed by the Centers for Disease Control and Prevention 2012/2014, which facilitate a quick overview of the effectiveness of preventive measures that can be developed. HAI and anatomical localization are established based on standard definitions. Standard criteria should be reviewed and approved by the hospital’s infection control committee (Emori & Gaynes, 1993; Kluytmans–VandenBergh et al., 2005). Many patients receive antimicrobial drugs; through selection and exchange of genetic resistance elements, antibiotic pressure promotes the emergence of multi-resistant bacterial strains (Jarvis, 1996; World Health Organization, 2002), defined as resistance to more than three classes of antibiotic (Dent et al., 2010). Several reports have emphasized the development of antibiotic resistance among Gram-negative bacilli, especially Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterobacter spp. (Vasudevan et al., 2014). These organisms are increasing in incidence among nosocomial pathogens, largely because of their ability to express certain resistance phenotypes (Emori & Gaynes, 1993); antibiotics exert selection pressure on infectious agents and alter the bacterial ecology of each medical centre.

Patients in long-term care facilities are also frequently colonized (Chong et al., 2013; Han et al., 2012), with extended-spectrum β-lactamase (ESBL)-producing bacteria (O’Brien & Stelling, 2011; Thaden et al., 2015) that have the ability to break down commonly used antibiotics.

Since January 2011, following the intensification of the signals of microbiological SE (alert micro-organism) and the detection of Klebsiella ESBL+ in seven cultures, collected over 7 days from five patients in the neurosurgical division (NCH1), the Foundation IRCCS Neurological Institute Carlo Besta has established a protocol for prevention and control of HAI by collecting surveillance data, with the main objective being to ensure epidemiological surveillance of infections within the same structure and to start promptly, if necessary, the relative procedures. The Besta Neurological Institute is a regional and national centre of excellence for the treatment of neurological diseases (223 beds), with an average of 6581 admissions, over 274 000 outpatients and 2500 neurosurgery procedures per year. The foundation treats oncological, degenerative and rare neurological diseases affecting both children and adults. It is highly active in the field of neurosurgery and carries out clinical and basic research to improve treatment and diagnosis.

The main goal of this study was to establish monitoring of SE in order to:

- identify infection factors;
- define the priorities and the most effective preventive measures;
- take efficient action in the fight against HAI;
- define the necessary precautions to be implemented;
- avoid renewal of these precautions, and the evaluation of actions taken to reduce risk factors;
- assess the epidemiological occurrence of multi-resistant bacteria and attempt to identify preventive actions.

METHODS

Study design. The procedure is aimed at formalizing the management mode and the reporting and transmission of SE. A cohort study with retrospective data (i.e. in which data on SE and determinants, including interventions decided independently of this study, were collected at the end of study period for previous years) was performed to examine the incidence of SE from 1 January 2012 to 31 December 2014.

Setting. The study was performed at the Fondazione IRCCS Istituto Neurologico Carlo Besta, and was approved by the local ethics committee (protocol no. 25E/24/2015).

Participants. The sample included patients of all ages affected by different neurological and neurosurgical pathologies, particularly the selection criteria of patients carrying multidrug resistance (MDR) or with specific resistance.

For infection control measures and procedure regarding the incidence of SE, the following points were considered:

- microbiological and epidemiological information on SE;
- analysis of the factors that are determinants for the occurrence of the same events;
- individuation of SE and implementation of surveillance measures;
- checking the effective implementation of preventive actions and their effectiveness;
- notification of SE to departments when micro-organisms are isolated;
- use of checklist protocol for HAI prevention;
- systematic use of nebulizers;
- appropriate environmental sanitation and disinfection of medical equipment;
- implementation of specific procedures for specific micro-organisms;
- evaluation of the assessment of actions taken to reduce risk factors.

Outcome (SE) definitions. The outcome definitions are as follows: (1) microbiological surveillance after negativization of cultural examination and (2) evaluation of the assessment of actions taken to reduce risk factors and the fact that any antibiotic administration exerts selection pressure, modifying the bacterial sensitivity profile and promoting the acquisition of resistant and infectious organisms.

Assessment and microbiological assessment. Based on the type and site of infection, clinical specimens such as pus/exudates, blood and...
involved in hospital infections were broad-spectrum tam producers (ESBL+), and all bacterial isolates, except for 1000 in 2013 and 2012, respectively); the 4.38/1000 admissions in 2014 versus 3.85/1000 and 1.70/1000 admissions (128 patients) and 9.3/1000 admissions (60 patients), respectively (Table 1) (both P<0.001 with respect to 2013).

In 2014, we noted an increase in the rate of Escherichia coli 4.38/1000 admissions in 2014 versus 3.85/1000 and 1.70/1000 admissions (128 patients) and 9.3/1000 admissions (60 patients), respectively (Table 1) (both P<0.001 with respect to 2013).

In 2014, we noted an increase in the rate of Escherichia coli 4.38/1000 admissions in 2014 versus 3.85/1000 and 1.70/1000 admissions (128 patients) and 9.3/1000 admissions (60 patients), respectively (Table 1) (both P<0.001 with respect to 2013).

Statistical methods. Categorical variables were described by counts and percentages as mean and SD or median and interquartile range. The incidence rates (IRs) of SE were calculated per 1000 patient-days for 100 admissions [with relevant 95% confidence intervals (CIs)] using Poisson distribution. The Poisson regression model was used to analyse both the temporal trend and associations among age, sex, patient-day and hospitalization within 30 days of the previous analysis. The results are expressed as IR ratio (IRR) with 95% CIs. P<0.05 was considered statistically significant, and all tests were two-sided. Data analysis was performed with the Stata statistical package (release 14, 2015; Stata Corporation).

RESULTS

It is recorded that, of a total of 6080 hospitalizations detected up to 31 December 2014, the number of isolations was significantly reduced; in particular, the rates of patients carrying MDR micro-organism or with specific resistance decreased to 8.8/1000 admissions (54 patients) compared to the rates found in 2013 and 2012 which were 20.56/1000 admissions (128 patients) and 9.3/1000 admissions (60 patients), respectively (Table 1) (both P<0.001 with respect to 2013).

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Table 1. Rates of patients carrying multi-resistant micro-organisms or microorganisms with specific resistance, 2012–2014

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of admissions</th>
<th>No. of SE</th>
<th>Rate SE/1000 admissions</th>
<th>No. of isolations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>6391</td>
<td>60</td>
<td>9.3</td>
<td>145</td>
</tr>
<tr>
<td>2013</td>
<td>6223</td>
<td>128</td>
<td>20.56</td>
<td>261</td>
</tr>
<tr>
<td>2014</td>
<td>6080</td>
<td>54</td>
<td>8.88</td>
<td>100</td>
</tr>
</tbody>
</table>

In 2014, we detected one case of pulmonary aspergillosis but no cases of Candida isolation; only one case of Clostridium difficile infection was detected in an immunocompromised neurological patient subjected to numerous antibiotic therapies, as well as a single isolation, from urine culture, of K. pneumoniae (rate 0.28/1000 admissions).

In 2014, 82% of Gram-negative bacteria (mainly Enterobacteriaceae) transmitted by contact were isolated, and the data for 2012/2013 were comparable. This result is directly dependent on healthcare assistance.

The strict control carried out and the implementation of measures to prevent or contain Acinetobacter baumannii, which was the primary cause found in our department of HAI MDR in 2012, have ensured a reduction in the incidence of the same; however, this species remained one of the main micro-organisms involved in the department in 2013. Monitoring in 2014 showed a sharp reduction in the rate (2.90 isolates/1000 admissions in 2012, 5.46/1000 in 2013 and 0.49/1000 in 2014) (both P<0.001). Eight patients

Table 2. MDR rates Regione Lombardia and Istituto Neurologica Besta, Italy, 2012/2013

<table>
<thead>
<tr>
<th>Years</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli ESBL+</td>
<td>6.24*</td>
<td>8.54*</td>
</tr>
<tr>
<td>K. pneumoniae ESBL+</td>
<td>2.09†</td>
<td>2.70*</td>
</tr>
<tr>
<td>S. aureus MRSA</td>
<td>5.64*</td>
<td>6.20*</td>
</tr>
</tbody>
</table>

Data from 44 hospitals. Data for 2014 not yet available.  
*Regione Lombardia, Italy.  
†Istituto Neurologico Besta.
were carriers of *A. baumannii*, none of whom were treated with colistin because we considered the micro-organism as colonizing and not responsible for infectious diseases. All patients carrying this micro-organism were admitted to the hospital in the first half of 2014 (Lo et al., 2014); 54 patients were subjected to isolation for a total of 1008 days of hospitalization, with an average period of isolation of 17 days (minimum, 1 day; maximum, 134 days). In 12 patients, the isolation period was less than 1 week; in these patients, clinical conditions were considered adequate to allow home discharge or to transfer to a rehabilitation facility. Only four patients underwent an isolation period of more than 3 months, those suffering from severe neurological deficits through chronic neurological pathologies, or those with post-surgical complications.

**Table 3. Key microbiological SE involved, 2012–2014**

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>Rate per 1000 hospitalizations, 2012 (n=6391)</th>
<th>Rate per 1000 hospitalizations, 2013 (n=6223)</th>
<th>Rate per 1000 hospitalizations, 2014 (n=6080)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. baumannii</em></td>
<td>2.90</td>
<td>5.46</td>
<td>0.49</td>
</tr>
<tr>
<td>Acinetobacter <em>junii</em> ertapenem-R</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Burkholderia</em> capacia</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>E. coli</em> ESBL+</td>
<td>1.70</td>
<td>3.85</td>
<td>4.38</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> KPC or ESBL or MDR</td>
<td>1.70</td>
<td>1.12</td>
<td>0.16</td>
</tr>
<tr>
<td>Proteus <em>mirabilis</em> ESBL+</td>
<td>0.15</td>
<td>0.32</td>
<td>–</td>
</tr>
<tr>
<td><em>Providencia stuartii</em></td>
<td>0.15</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>P. aeruginosa</em> KPC or MDR</td>
<td>0.46</td>
<td>0.48</td>
<td>7.08</td>
</tr>
<tr>
<td><em>Salmonella</em> group</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>–</td>
<td>0.48</td>
<td>0.33</td>
</tr>
<tr>
<td><em>Staphylococcus</em> capitis</td>
<td>–</td>
<td>0.32</td>
<td>–</td>
</tr>
<tr>
<td><em>Staphylococcus</em> haemolyticus</td>
<td>0.31</td>
<td>0.96</td>
<td>–</td>
</tr>
<tr>
<td><em>Staphylococcus</em> hominis</td>
<td>0.46</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Staphylococcus</em> sciuri</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Staphylococcus</em> warneri</td>
<td>–</td>
<td>0.32</td>
<td>–</td>
</tr>
<tr>
<td><em>Staphylococcus</em> epidermidis</td>
<td>0.31</td>
<td>2.41</td>
<td>0.16</td>
</tr>
<tr>
<td><em>Staphylococcus</em> aureus Oxacillin</td>
<td>0.46</td>
<td>2.09</td>
<td>2.02</td>
</tr>
<tr>
<td><em>C. difficile</em></td>
<td>0.31</td>
<td>–</td>
<td>0.16</td>
</tr>
<tr>
<td><em>Corynebacterium</em> species</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><em>Corynebacterium</em> striatum</td>
<td>–</td>
<td>0.16</td>
<td>–</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8.91</strong></td>
<td><strong>19.41</strong></td>
<td><strong>14.78</strong></td>
</tr>
</tbody>
</table>

**Mycetes**

| *Aspergillus fumigatus* | –                                      | –                                             | 0.33                                          |
| *Candida albicans* | –                                      | 0.16                                          | –                                             |

were carriers of *A. baumannii*, none of whom were treated with colistin because we considered the micro-organism as colonizing and not responsible for infectious diseases. All patients carrying this micro-organism were admitted to the hospital in the first half of 2014 (Lo et al., 2014); 54 patients were subjected to isolation for a total of 1008 days of hospitalization, with an average period of isolation of 17 days (minimum, 1 day; maximum, 134 days). In 12 patients, the isolation period was less than 1 week; in these patients, clinical conditions were considered adequate to allow home discharge or to transfer to a rehabilitation facility. Only four patients underwent an isolation period of more than 3 months, those suffering from severe neurological deficits through chronic neurological pathologies, or those with post-surgical complications.

**Total isolations/1000 Length of Stay**

Overall, 242 SE were detected: 60, 128 and 154 in 2012, 2013 and 2014, respectively (Table 1). With regard to the individual units surveyed during the study period, 70 SE were detected in surgical units, 77 in neurological non-surgical units, 11 in paediatric units, 73 in intensive care units and 4 in outpatient departments. Considering the entire observational period, the IR of isolation for 1000 patient-days varies from a minimum of 0.52 (95 % CI, 0.23–1.15) in the second quarter of 2014 to the maximum value of 4.16 (95 % CI, 3.20–5.40) in the first quarter of 2013 (*P*<0.01 with respect to all other trimesters), followed by a decrease from the third quarter of 2013 which remained constant throughout 2014, reaching values similar to those of 2012 (Fig. 1).

The year 2013 was initially characterized by an eightfold increase in the rate of isolation, and subsequently by a marked oscillation of isolation rate. Regarding individual departments, during all four quarters of 2012 the rate of isolation remained constant for paediatric units (IR between 0.0 and 0.5) and for neurological/medical units (IR oscillating around 1.0), while surgical departments showed a
decrease from 2.2 (95% CI, 1.2–4.1) to 1.2 (95% CI, 0.41–3.1) (although not significant, $P=0.82$).

Data show that between the end of 2012 and the first quarter of 2013, there was a significant increase in all departments surveyed. For medical/neurological units, there was an increase in the isolation rate of 1.9 per 1000 patient-days. This peak was followed by a decrease in the rate in medical units (from 3.1 to 1.1) ($P=0.04$) and intensive care units (from 8.7 to 5.9).

Moreover, paediatric units showed an increase from 0 to 2.4 in the isolation rate (third quarter of 2013), followed by either a decrease or no isolation rate until the end of the period under study.

From the third quarter of 2013 until the end of the study, surgical and medical department showed relatively low rates of isolation, within a range ≤1.20 and similar to 2012, except for intensive care units that, although showing a decreasing rate, in the penultimate and final quarters of 2014 had rates of 2.1 and 1.1, respectively.

### Isolations/100 admissions

The rates of isolation per 100 admissions appear to be similar to the rates of isolation per 1000 patient-days, and are shown in Fig. 2.

### Factors related to SE

SE were associated with age (per 10-year increment: IRR, 1.11; 95% CI, 1.05–1.17; $P<0.001$); admission ward (surgery vs paediatrics: IRR, 4.17; 95% CI, 2.21–7.84; non-surgical vs paediatrics: IRR, 3.39; 95% CI, 1.81–6.39; $P<0.001$); new admission within 30 days of previous discharge (yes vs no: IRR, 2.81; 95% CI, 1.88–4.19; $P<0.001$); and patient-days (per 5-day increment: IRR, 1.14; 95% CI, 1.13–1.15; $P<0.001$); but not with gender (M vs F: IRR, 0.87; 95% CI, 0.68–1.12; $P=0.284$).

### DISCUSSION

The implementation of microbiological monitoring of SE led to the adoption of a series of actions, including isolation and precautions. In 2011, all healthcare staff were informed of the importance of addressing the problem of dispersal of infections through contact, and of the importance of hand washing. The results of our epidemiological survey show that, in
the years monitored, the most significant microbiological SE are those in the department of neurosurgery (intensive care and neurosurgical For the most part, these patients underwent central venous and urinary catheterization with compromised general and neurological conditions, and in these cases antibi-otic pressure was high.

At the end of the study, the corrective actions or control measures that we carried out were as follows:

- Improvement in communication regarding microbiolog-ical SE; placing the data in a logistical/chronological database updated daily and readily available, showing the status of patients in isolation.
- Improved methods of sanitation and disinfection of spaces and surfaces as the predominant finding of micro-organism spread by contact; a hydrogen peroxide nebulizer was purchased for decontamination of surfaces as part of the systematic sanitation and disinfection of hospital rooms.
- Adherence to regional innovative/informatics solutions for epidemiological control on the spread of microbiolog-ical sentinel agents.
- The feasibility of setting up a system of partitioning of rooms was taken into consideration: rooms dedicated to achieving negative/positive pressure which would prevent the exit of pathogens.
- Positive feedback from training medical/nursing staff delivered at various levels for the entire preceding year, while taking into account the latest guidelines in regard to infections related to assistance (ICA) and the imple-mentation of the sepsis protocol according to the guidelines of the Sepsis Surviving Campaign 2012/2014 (Dellinger et al., 2013).
- Consolidation of an of antibiotics policies, characterized by antibiotic selection and the implementation of de-escalation (Christoff et al., 2010).

A criticism of the procedure undertaken is represented by the area of patient isolation, which was suitable only for patients who could be managed in neurosurgical departments; in most cases, microbiological SE were identified in patients hospitalized in the intensive care unit (Monnet, 2000; Vincent et al., 1995).

The main study limitation is related to data collection, which was carried out in a rather inhomogeneous way in 2012. A further limitation is the acquisition of innovative/logistic solutions for controlling the spread of microbiolog-ical SE in 2012. In 2013, this was noted as overtreatment of patients in our efforts to control SE.

The predominant population of Gram-negative SE makes it clear that transmission is predominantly by contact, and thus the difficulty is in maintaining good hygiene practices. However, implementation of measures to prevent or contain A. baumannii, the primary cause in our division of MDR infections in 2012, and often associated with co-infection, has ensured a reduction in the incidence of this micro-organism (Fig. 3).

Recent data show that 36% of the strains of E. coli, Gram-negative organisms mainly involved in hospital infections, are fluoroquinolone resistant (van de Sande-Bruinsma et al., 2008). In humans, K. pneumoniae can colonize differ-ent tissues of the body (Johnson et al., 2008) and often

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**Fig. 3.** MDR rate per 1000 admissions from 2012 to 2014.
## Table 4. Antimicrobial drug sensitivity

<table>
<thead>
<tr>
<th>Strain/Species</th>
<th>Amoxicillin</th>
<th>Amoxicillin/Clavulanate</th>
<th>Cefotaxim</th>
<th>Ceftriaxone</th>
<th>Ciprofloxacin</th>
<th>Enrofloxacin</th>
<th>Gentamicin</th>
<th>Imipenem</th>
<th>Meropenem</th>
<th>Nitrofurantoin</th>
<th>Nitrofurathine</th>
<th>Oxacillin</th>
<th>Pencillin G</th>
<th>Rifampicin</th>
<th>Teicoplanin</th>
<th>Tobramycin</th>
<th>Trimethoprim/Sulfamethoxazole</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>96%</td>
<td>82%</td>
<td>76%</td>
<td>89%</td>
<td>67%</td>
<td>57%</td>
<td>82%</td>
<td>88%</td>
<td>92%</td>
<td>100%</td>
<td>100%</td>
<td>57%</td>
<td>69%</td>
<td>67%</td>
<td>76%</td>
<td>99%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>93%</td>
<td>93%</td>
<td>88%</td>
<td>94%</td>
<td>96%</td>
<td>92%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
<td>58%</td>
<td>61%</td>
<td>67%</td>
<td>77%</td>
<td>98%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>95%</td>
<td>95%</td>
<td>90%</td>
<td>92%</td>
<td>92%</td>
<td>88%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
<td>57%</td>
<td>61%</td>
<td>67%</td>
<td>77%</td>
<td>98%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>69%</td>
<td>59%</td>
<td>73%</td>
<td>83%</td>
<td>88%</td>
<td>88%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
<td>58%</td>
<td>61%</td>
<td>67%</td>
<td>77%</td>
<td>98%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>95%</td>
<td>95%</td>
<td>90%</td>
<td>92%</td>
<td>92%</td>
<td>88%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
<td>57%</td>
<td>61%</td>
<td>67%</td>
<td>77%</td>
<td>98%</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td>95%</td>
<td>95%</td>
<td>90%</td>
<td>92%</td>
<td>92%</td>
<td>88%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
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Legend
- \( \text{ls} \) = low sensitivity \(< 55\%\)
- \( \text{h} \) = high sensitivity \( \geq 95\%\)

Fluconazole: 100%
ACKNOWLEDGEMENTS

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REFERENCES


