pathogen among healthcare workers [4], as observed in this study. A lack of experience on how to approach and manage cases remains a major challenge in unaffected countries. Informational and educational tools are required, particularly in cardiothoracic centres.

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Evaluation of microbiological screening in a neonatal intensive care unit to optimize empiric antibiotic use

Sir,

Bacterial infections are a major cause of morbidity and mortality in newborn infants, and treatment with an appropriate antibiotic agent is essential. Bacteria causing nosocomial infections colonize the patient's mucosa and gastrointestinal tract prior to an infection [1]. We implemented screening for colonizing bacteria that were considered in deciding on empiric antibiotic therapy and evaluated the implications of such microbiological screening for clinical practice.

All inpatients hospitalized for at least three days in our tertiary care neonatal intensive care unit (NICU) were systematically screened with weekly pharyngeal and rectal swabs over 22 months. The swabs were analysed using routine methods by the clinical microbiology laboratory at our University Medical Center. Target bacteria were: (i) multidrug-resistant (MDR) bacteria: meticillin-resistant *Staphylococcus aureus* (no patients), vancomycin-resistant enterococci (no patients), and multidrug-resistant Gram-negative bacteria: MDR *Klebsiella pneumoniae* (six patients), MDR *E. coli* (six patients), and MDR *Enterobacter cloacae* (nine patients); (ii) bacteria causing invasive infections: *Acinetobacter* spp. (six patients), *Klebsiella pneumoniae* (eight patients), *Staphylococcus aureus* (12 patients); (iii) highly pathogenic bacteria: *Serratia marcescens* (three patients), *Pseudomonas aeruginosa* (five patients), and *Enterobacter* spp. (30 patients). *Enterobacter* spp. are known to develop resistance to third-generation cephalosporins during antibiotic therapy due to inducible resistance genes and were thus considered potentially to be MDR. Of 204 included patients, 83 had a gestational age $<$32 weeks and 85 a birth weight $<$1500 g. Sixty out of 204 patients (29%) were colonized with one to five different target bacteria. The most frequently isolated bacteria in our NICU and the occurrence of MDR are comparable to other reports [2,3]. Three clusters of colonized patients (definition: $\geq$4 patients colonized simultaneously) were recorded: two clusters of *Enterobacter* spp. and one cluster of ESBL-producing *E. coli*. None of these clusters of colonized patients was followed by clusters of infectious episodes. Clinically undetected clusters have been described previously and probably occur repeatedly [4,5]. Episodes of nosocomial infection were defined as invasive infections occurring after 72 h of admission (Table I). Primary sepsis, necrotizing enterocolitis, and pneumonia were recorded according to previously described case definitions [7]. Peritonitis was defined as clinical symptoms and laboratory changes as for sepsis plus positive peritoneal culture. Standard empiric treatment for nosocomial infection consisted of cefotaxime and vancomycin. Patients colonized with MDR or potential MDR were treated with meropenem and vancomycin. Patients colonized with *Pseudomonas aeruginosa* were treated with ceftazidime. The incidences of infection in infants with a birth weight $<$1500 g were low: bloodstream infection (BSI) 12%, Gram-negative BSI 0.5%, and MDR-related infection 0.5%. Three episodes of infections were attributed to bacteria previously identified by the screening. The patient who suffered from a BSI due to *P. aeruginosa* was colonized with three different bacteria prior to the infection: MDR *Klebsiella pneumoniae*, *Enterobacter cloacae* and *P. aeruginosa*. He was treated with third-generation antibiotics vancomycin and meropenem until the blood culture result revealed *P. aeruginosa*. The other two patients were not colonized with other relevant bacteria. A further 17 out of 44 episodes of nosocomial infection occurred in nine patients on whom MDR or potentially MDR had been detected previously. These nine patients received meropenem as adapted empiric antibiotic therapy during 16 episodes of nosocomial infection. In one episode, meropenem was not used. Three of 204 resistant pathogen-colonized patients suffered from a nosocomial infection caused by bacteria that were previously identified by the screening programme, and we

Table I
Episodes of nosocomial infections from July 2012 to April 2014

Type of infection	Episodes in patients ≥1500 g	Episodes in patients <1500 g	Identified bacteria causing infection	Bacteria previously identified by the screening?
Primary sepsis				
Clinical sepsis[a]	6	18	—	No
BSI CoNS only[b]	2	8	CoNS	Not screened for
BSI[c]	—	1	*Pseudomonas aeruginosa*	Yes
	—	1	*Staphylococcus aureus*	No
Peritonitis	—	1	*Enterobacter cloacae* MDR	Yes
Urinary tract infection	—	1	—	No
Necrotizing enterocolitis	1	2	—	No
Pneumonia	—	1	*Pseudomonas aeruginosa*	Yes
	1	1	—	No

BSI, bloodstream infection; CoNS, coagulase-negative staphylococci; MDR, multidrug-resistant.
Total of 44 episodes of nosocomial infections in 32 patients.
[a] Clinical sepsis with negative blood cultures.
[b] Laboratory confirmed BSI with CoNS as sole pathogen.
[c] Laboratory confirmed BSI with detection of pathogens other than CoNS.

believe these patients may have benefited by receiving prospectively identified susceptible antibiotics when treatment was implemented. However, there are several concerns associated with this approach, including:

- The fact that 16 episodes of infection in nine patients colonized with MDR or possible MDR were treated with third-line antibiotics as empiric antibiotic therapy, without proof that the colonizing bacteria were causative, suggests that detection of MDR or possible MDR bears a significant risk of unnecessary use of third-line antibiotics.
- Colonization by more than one Gram-negative bacterium prior to infection is not unusual and was found in 19 patients of our cohort [1,8]. Thus, colonization by several resistant pathogens makes it impossible to know which pathogen might require targeted antimicrobial therapy. Consequently, it is frequently not possible to use prospective colonizing pathogen antibiotic susceptibility in any of these patients.
- The detecting colonizing potential MDR pathogens may not be identified due to the gap between weekly specimen collections.
- The fact that Gram-negative BSI and MDR-related infections are rare provides an additional bias intrinsically limiting the value of this type of screening programme.

Furthermore, we believe that implementation of a microbiological screening programme to assess the impact on mortality and morbidity in NICU patients has yet to be studied and could be the basis for a randomized controlled trial.

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Workplace vaccination against measles in a teaching hospital of Rome

Sir,

Measles is an acute, highly contagious infectious disease caused by a virus belonging to the Parvomyxoviridae family [1]. Two doses of measles vaccine (effectiveness 99%) are considered to provide long-lasting immunity even if antibody levels decline over time [2]. However, measles outbreaks continue to occur in countries with high vaccination coverage, suggesting an immune gap in the involved populations.

In 2017, Italy reported the second highest rate of measles infection among the European Countries (4,991). In particular, Lazio Region (the Region including Rome district) reported the highest number of cases (1,699) among Italian Regions. As far as the prevalence among healthcare workers (HCWs) is concerned, a total of 322 cases were reported in 18 out of 20 Italian Regions [3]. The epidemiological aspects of this outbreak can be explained by the low vaccination coverage recorded for measles, mumps and rubella (MMR).

A study performed in Italy from 1st January to 31st August 2017 showed that 22.3% of measles infection were detected in hospital settings and 6.6% of cases occurred in HCWs [4]. Other studies among HCWs demonstrated that 4—10% of all hospital workers lacked specific measles-specific Immunoglobulin G (IgG) antibodies [5]. In a previous study, we found non-protective measles-specific IgG antibody titres in a substantial percentage of HCWs, especially those younger than 35 years of age [6].

In order to avoid nosocomial measles outbreaks, we investigated the immunity status and vaccination attitude towards measles of HCWs at the teaching hospital Polyclinic Tor Vergata (PTV) of Rome. The same investigation was performed in students of the Medical Area of the University of Rome Tor Vergata, who carried out health surveillance at the Occupational Medicine ambulatory between 1st January and 31st December 2017. Measles-specific IgG antibodies were measured in serum by means of a chemiluminescent test (DiaSorin LIASON® Measles IgG assay). Subjects with measles-specific antibodies higher than 16.5 AU/mL were considered serologically immune. HCWs who documented a two-dose vaccination with MMR were considered protected, independently from their antibody titre, in accordance with the Centers for Disease Control and Prevention (CDC) guideline [1].

MMR vaccine was offered for free to all HCWs and students with measles-specific antibody serum value below than 16.5 AU/mL without a documented vaccination with two doses.

The aim of the study was to assess vaccine compliance and the effectiveness of workplace vaccination in reducing the risk of infection.

A total of 2,941 subjects (964 men and 1977 women) were included; 1772 (60.25%) were HCWs and 1,169 (39.75%) students of the Medical Area. The mean age of the general population was 32.89 years (standard deviation (SD) 10.8). According to age, we stratified included subjects in three groups: <35 years (77.30% serologically immune and 22.77% serologically not immune); between 35 and 55 years (97.19% serologically immune and 2.81% serologically not immune); >55 years (99.21% serologically immune and 0.79% serologically not immune). As a whole, 450/2,941 (15.30%) were serologically non-immune to measles; among these, 77 had been previously vaccinated with two doses of measles vaccine and therefore were considered immune to the disease even in the absence of protective titre. The vaccination campaign was addressed to the remaining 373 subjects.

A total of 178/373 (47.72%) subjects agreed to be vaccinated with MMR vaccine. Agreement was higher in the male gender (70/138, 50.72%) compared to the female gender (108/235, 45.96% $P < 0.05$).

Workplace vaccination proved effective in controlling infection among HCWs. In fact, despite the vaccination uptake being below 50%, the percentage of immune subjects reaching 90% coincided with no new cases of measles among HCWs (Figure 1).

We feel that the exact definition of the target of the vaccination campaign, provision of information about the risks of measles, and the ready availability of the vaccine minimized the expected 'vaccine hesitancy' [7].

HCWs below the age of 35 years showed the highest percentage of subjects susceptible to measles (15.30%). They represent the subjects born between 1982 and 1999 when the vaccination coverage against measles was inadequate [6]. All cases that occurred among the HCWs during 2017 (21 subjects) concerned the age group under 35 years. Therefore, this age group can be considered as the true high-risk group in our population.

In order to achieve the highest adherence to vaccination, we implemented, in collaboration with the Health Direction,

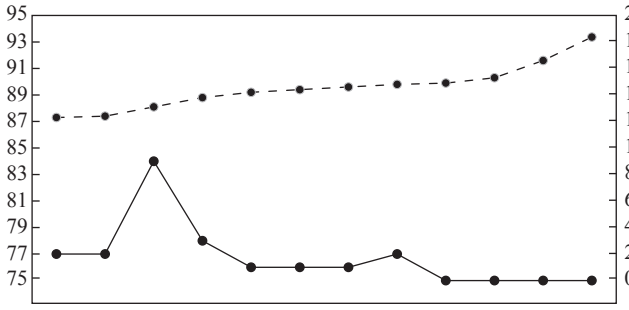

Figure 1. Occurence of measles cases in healthcare workers in relation to proportion of healthcare workers who were measles immune.