

# Distribution of Nosocomial Organisms and their Resistance Patterns in the Intensive Care Unit of the University Hospital of the West Indies, Kingston, Jamaica

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## ABSTRACT

**Objectives:** To determine the distribution and antibiotic susceptibility patterns of nosocomial pathogens in the Intensive Care Unit (ICU) at the University Hospital of the West Indies (UHWI).

**Methods:** A retrospective review of the laboratory records of all ICU patients from 2002–2004 was done. All organisms isolated from blood, urine, sputum, wound swabs and CVP tips were recorded. Sensitivity reports for organisms isolated in 2004 were also obtained. Results were analysed according to source of isolates and type of infection.

**Results:** Gram-negative organisms account for the majority of ICU isolates and show resistance to multiple antibiotics. The common Gram negative pathogens in the ICU are *Pseudomonas aeruginosa*, *Acinetobacter* spp and *Stenotrophomonas maltophilia* while the common Gram positive nosocomial organisms are Group D Streptococcus and coagulase negative Staphylococcus.

**Conclusion:** The organisms isolated in the ICU at the UHWI are similar to those isolated in many ICUs all over the world. Surveillance data are necessary to monitor nosocomial pathogens and their resistance patterns to guide empirical antibiotic therapy.

# Distribución de los Organismos Nosocomiales y sus Patrones de Resistencia en la Unidad de Cuidados Intensivos del Hospital Universitario de West Indies, Kingston, Jamaica

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## RESUMEN

**Objetivos:** Determinar la distribución y los patrones de susceptibilidad antibiótica de los patógenos nosocomiales en la Unidad de Cuidados Intensivos (UCI) del Hospital Universitario de West Indies (HUWI).

**Métodos:** Se realizó una revisión retrospectiva de las historias clínicas de laboratorio de todos los pacientes de la UCI de 2002–2004. Se registraron todos los organismos aislados a partir de sangre, orina, esputo, hisopos de heridas, y las puntas de catéteres de PVC. Los resultados fueron analizados de acuerdo con las fuentes de los aislados y el tipo de infección.

**Resultados:** Los organismos gramnegativos representan la mayor parte de aislados de la UCI y muestran resistencia a múltiples antibióticos. Los patógenos gramnegativos comunes en la UCI son *Pseudomonas aeruginosa*, *Acinetobacter* spp y *Stenotrophomonas maltophilia* mientras que los organismos nosocomiales grampositivos comunes son Group D Streptococcus y coagulase negative Staphylococcus.

**Conclusión:** Los organismos aislados en la UCI en el HUWI son similares a los aislados en muchas UCIs en todo el mundo. La información sobre la vigilancia es necesaria a fin de monitorear los patógenos nosocomiales y sus patrones de resistencia para guiar la terapia antibiótica empírica.

West Indian Med J 2009; 58 (2): 142

## INTRODUCTION

Infections in Intensive Care Units are a source of great concern globally because of their impact on patient morbidity and mortality as well as their impact on the cost of patient care. One important feature of these infections which continues to pose a therapeutic challenge is the increasing resistance to multiple antibiotics. It is internationally accepted that the most resistant organisms often appear first in the Intensive Care Unit where patients are debilitated, very often have multiple lines and tubes and have been exposed to a wide array of antibiotics. The driving forces for antimicrobial resistance include poor infection control practices and the overuse/misuse of antibiotics (1). The emergence of organisms that are resistant to all the antibiotics usually used against them (pan-resistant) is alarming. This situation becomes even more grim because relatively few new antibiotics with activity against Gram negative bacteria are being developed. The need to use the available antibiotics wisely, in order to maximize their impact and prolong their usefulness, cannot be overemphasized. It is therefore important to know the local antibiotic resistance patterns as these may differ from other settings and is required to inform appropriate local antibiotic use. In order to control the spread of resistant bacteria, local surveillance data should play an integral role in developing effective intervention strategies (2).

Gram negative bacilli continue to be the leading cause of serious infections especially in hospital settings. The more commonly implicated organisms include *Pseudomonas aeruginosa*, *Acinetobacter calcoaceticus-baumannii*, *E coli*, *K pneumoniae* and at the University Hospital of the West Indies (UHWI), Jamaica, *Stenotrophomonas maltophilia* has emerged as a significant nosocomial pathogen in the ICU (3). The tendency for Gram negative bacilli to become resistant to multiple antimicrobials has been duly noted (4). There are both co-resistant and cross-resistant mechanisms conferring resistance to multiple antibiotics (5). *Pseudomonas aeruginosa* isolates, for example, can have extended spectrum beta-lactamases (ESBL), Amp-C beta-lactamases, aminoglycoside modifying enzymes which are co-resistant mechanisms and can therefore show resistance to most of the commonly used antibiotics (5). The presence of ESBL producers in the Enterobacteriaceae family can also confer resistance to multiple antibiotics. Cross-resistant mechanisms on the other hand have overlapping target sites or multidrug efflux pumps and this gives rise to resistance to many antibiotics. The MexA-MesB-OprM active efflux pump sometimes found in *Pseudomonas aeruginosa* isolates, for example, can lead to resistance to antibiotics such as beta-lactams, fluoroquinolones, macrolides, sulphonamides, tetracycline, trimethoprim, novobiocin and chloramphenicol (6).

While the emergence of resistance is thought to be due to a number of factors, some of which are poorly understood, there is compelling evidence to suggest causal association between antimicrobial usage in hospitals and antimicrobial

resistance. Some observations to support this include the fact that changes in antibiotic usage are paralleled by changes in the prevalence of resistance, increased prevalence of antimicrobial resistance in nosocomial bacterial strains when compared to community-acquired strains and areas within the hospital, such as the ICU, that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use (7).

In patients diagnosed with serious infections, there is a marked increase in mortality when inappropriate empiric antibiotic therapy is started initially compared with when the empiric antibiotic therapy started is appropriate (8–13). This underscores the importance of appropriate antibiotic guidelines in the ICU based on local data.

A knowledge of the organisms commonly implicated in specific infections and their antibiotic susceptibility patterns will allow for the selection of accurate empiric therapy to target the pathogens. Thus, a retrospective study was conducted to determine the organisms with their sensitivity patterns from patients in the ICU of the UHWI, Jamaica. This information can be used to develop guidelines to direct the antibiotic treatment of hospital acquired infections in the ICU.

## MATERIALS AND METHODS

A retrospective study of the records of all ICU patients for the period from January 2002–December 2004 was conducted. All microbiology results from blood, urine, sputum, wound swabs and catheter tips were collected. These were then analysed according to the type of infection caused. Antibiotic susceptibility patterns for the isolates collected in 2004 were determined from the records as well. Demographic and clinical data where necessary, were obtained from the patients' records.

Clinical specimens were plated on to culture media such as Blood and Macconkey agar and incubated at 37°C for 24-hours. Gram negative isolates were then identified using the automated VITEK system (bio Merieux) and Gram positive isolates were identified based on morphology and biochemical tests. Susceptibility testing of the isolates was done using a combination of the modified Kirby-Bauer disk diffusion method based on the guidelines from the Clinical and Laboratory Standards Institute (CLSI) and the automated VITEK system.

## RESULTS

A total of 1836 organisms was isolated from the Intensive Care Unit over the three year period. There were 1331 gram negative organisms accounting for 72.5% of the isolates while the Gram-positive cocci accounted for 27.5% with 505 isolates (Fig. 1).

Sputum yielded 724 isolates accounting for 40% of the total isolates followed by blood 639 (35%), urine 190 (10%), wounds 148 (8%) and CVP tips 135 [7%] (Fig. 2).

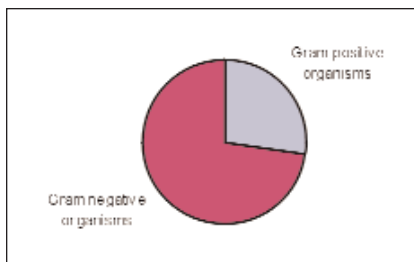


Fig. 1: The distribution of Gram positive and Gram negative organisms 2002–2004.

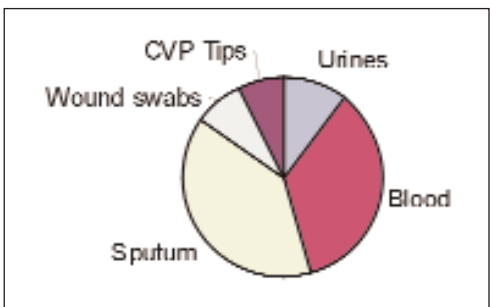


Fig. 2: The distribution of total isolates according to source 2002–2004.

The commonest Gram negative organism isolated was *Pseudomonas aeruginosa*, 344 isolates (25.8%) followed by *Acinetobacter spp* 316 (23.7%), then *Stenotrophomonas maltophilia* 255 (19.1%), *Klebsiella spp* 79 (5.9%), *Enterobacter spp* 71 (5.3%), *Pseudomonas spp* 67 (5%), *E coli* 63 (4.7%) and other Gram negative bacilli 136 [10.2%] (Fig. 3).

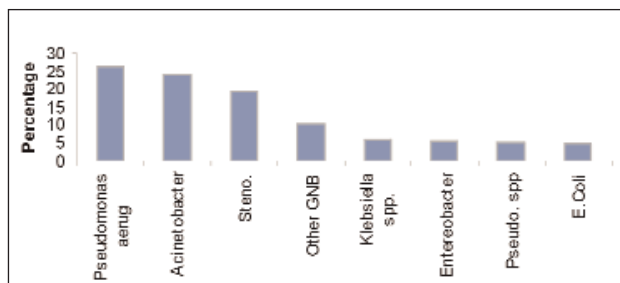


Fig. 3: The distribution of total Gram negative organisms 2002–2004.

Of the Gram positive cocci, *Coagulase negative Staphylococcus* was the commonest isolate 237 (46.9%), followed by *Group D Streptococcus* 197 (39%), *Staphylococcus aureus* 58 (11.5%) and other Gram positive cocci 13 [2.6%] (Fig. 4).

There was a decrease in *Acinetobacter spp* from 2002 to 2004 while *Stenotrophomonas maltophilia* and *Pseudomonas spp* increased. *Pseudomonas aeruginosa*, *E coli*, *Klebsiella spp* and *Enterobacter spp* remained at a consistent level (Fig. 5).

There was a decrease in *Coagulase negative Staphylococcus* in 2003 while *Group D Streptococcus* showed an increase in 2003 and *Staphylococcus aureus* showed a slight decrease in 2004 (Fig. 6).

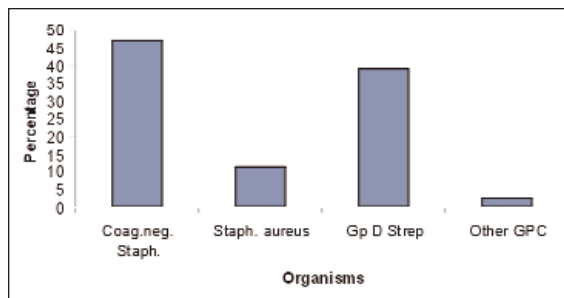


Fig. 4: Distribution of total GPC's: 2002–2004.

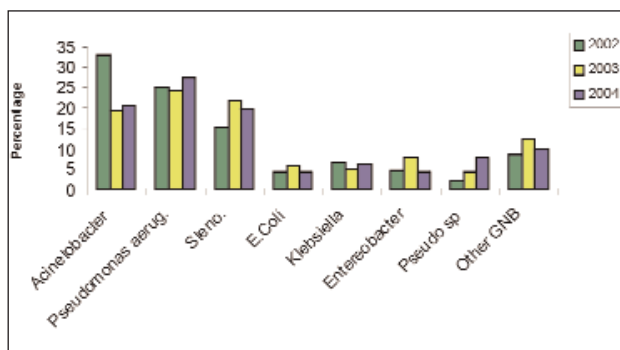


Fig. 5: Distribution of GNB's 2002–2004.

Fig. 6: Distribution of GPC's 2002–2004.

*Stenotrophomonas maltophilia* was the commonest isolate from blood increasing over the three years. *Pseudomonas aeruginosa* was the second most common isolate and while isolation of *Acinetobacter spp* decreased, *Pseudomonas spp* increased. *Coagulase negative Staphylococcus* was the commonest Gram positive isolate from blood followed by *Group D Streptococcus* (Fig. 7).

*Acinetobacter spp* and *Pseudomonas aeruginosa* were the commonest isolates from the sputum followed by *Stenotrophomonas maltophilia*. There was a marked increase in *Staphylococcus aureus* in 2003 which coincided with a *Staphylococcus aureus* outbreak in the ICU (Fig. 8).

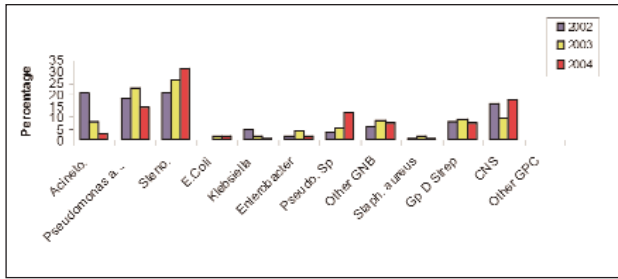


Fig. 7: Distribution of isolates from blood 2002–2004.

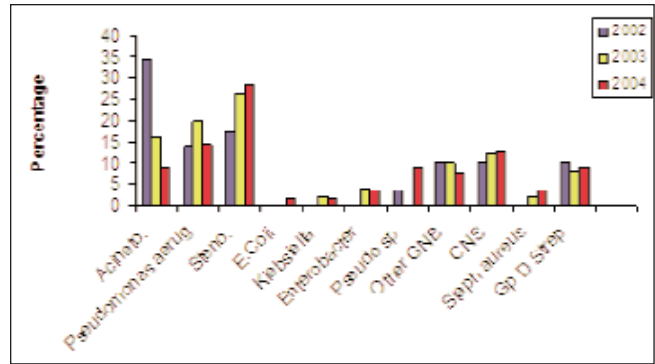


Fig. 10: Distribution of isolates from CVP tips 2002–2004.

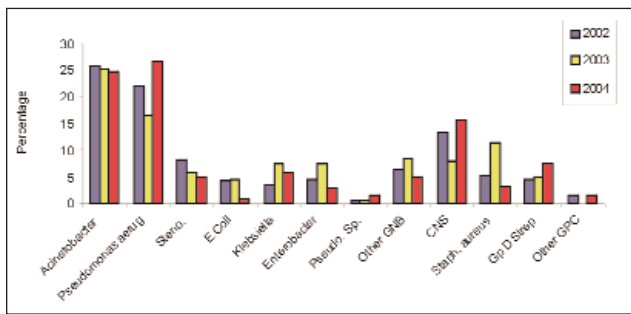


Fig. 8: Distribution of isolates from sputum 2002–2004.

*Group D Streptococcus* was the commonest isolate from the urine while *Acinetobacter spp.*, *E coli* and *Pseudomonas aeruginosa* were the most commonly isolated Gram negative isolates (Fig. 9).

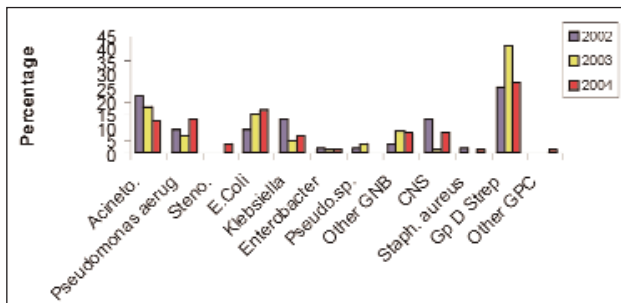


Fig. 9: Distribution of isolates from urine 2002–2004.

The pattern of distribution of *Stenotrophomonas maltophilia*, *Pseudomonas aeruginosa* and *Acinetobacter spp* isolated from CVP tips followed that of blood closely with *S maltophilia* increasing over the time while *Acinetobacter spp* decreased (Fig. 10).

*Group D Streptococcus* was the commonest isolate from wound swabs. *Coagulase negative Staphylococcus* was also commonly isolated even though there was a decrease in 2003. *Acinetobacter spp* and *Pseudomonas aeruginosa* were also commonly isolated.

Antibiotic resistance data collected for the more significant organisms in 2004 (Fig. 11) showed:

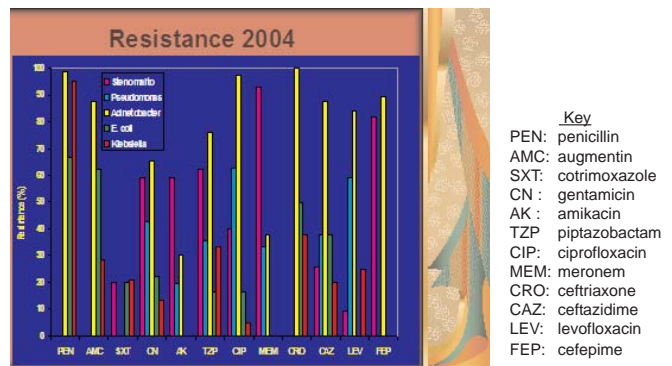


Fig. 11: Resistance 2004.

- C *Pseudomonas aeruginosa*: 63% resistant to ciprofloxacin, 59% to levofloxacin, 42% resistant to gentamicin, 20% to amikacin, 33% to meronem, 35% to piperacillin/tazobactam and 38% to ceftazidime.
- C *Stenotrophomonas maltophilia*: 93% resistant to meronem, 59% to gentamicin and amikacin, 62% to piperacillin/tazobactam, 40% to ciprofloxacin and 26% to ceftazidime
- C *Acinetobacter spp*: 97% resistant to ciprofloxacin, 89% to cefepime, 87% to amoxicillin-clavulanic acid and ceftazidime, 84% to levofloxacin, 76% to piperacillin/tazobactam, 66% to gentamicin, 38% to meronem and 30% to amikacin
- C *E coli*: 63% resistant to amoxicillin-clavulanic acid, 50% to ceftriaxone, 37.5% to ceftazidime, 22% to gentamicin, 20% to cotrimoxazole, 16.6% to piperacillin/tazobactam and ciprofloxacin. No resistance was seen to amikacin, meronem or levofloxacin.
- C *Klebsiella spp*: 37% resistant to ceftriaxone, 33% to piperacillin/tazobactam, 28% to amoxicillin-clavulanic acid, 25% to levofloxacin, 20% to ceftazidime, 14% to gentamicin and 5% to ciprofloxacin. There was no resistance to amikacin or meronem.

Gram positive isolates:

- C 88.9% of the *Staphylococcus aureus* isolates from the ICU in 2004 showed resistance to penicillin, 11.1% resistance to amoxicillin/clavulanic acid and 6.7% resistance to erythromycin while there was 100% sensitivity to methicillin and gentamicin. No resistance to vancomycin was detected.
- C 46.6% of coagulase negative *Staphylococcus* showed resistance to methicillin (MRSE). No resistance to vancomycin was detected.
- C Group D *Streptococcus* showed 75% resistance to gentamicin but only 3.9% and 3.3% resistance to ampicillin and amoxicillin-clavulanic acid respectively and no resistance to vancomycin.

## DISCUSSION

Microbial surveillance and knowledge of the prevailing resistance patterns are very important for every ICU. It has been observed that areas within hospitals that have the highest rates of antimicrobial use also have the highest rates of antimicrobial resistance (7). There are many factors causing patients in the ICU to be prone to bacterial infections. The use of lines and tubes which act as conduits for microbes across the defence mechanisms of the host facilitates the formation of biofilm which impairs the penetration of antibiotics thus protecting the microbes. The increased use of invasive devices and the performance of various types of surgery using prostheses also increase the introduction of microbes into an already compromised patient. In addition to these factors, healthcare workers at all levels are often guilty of inadequate hand-washing even though most will agree that it is the single most effective infection control measure.

The physical environment is also important as poorly cleaned wards allow an accumulation of dirt that can harbour resistant bacteria. (15). The presence of hot water in the ICU is an important infection control measure as many gram negatives such as *Pseudomonas aeruginosa* thrive in cold water but are destroyed by hot water. The absence of hot water in the ICU during the study period may have been a contributing factor to the high level of *Pseudomonas aeruginosa* which was the commonest Gram negative organism isolated. Many of the Gram negative isolates were from the sputum since many of the patients were on a ventilator and sputum samples are routinely sent to the laboratory. It is important to note that isolation of an organism does not necessarily indicate infection as the organism may simply be colonizing the area and the significance of an isolate should be determined using clinical and microscopic findings.

Unlike the Gram negative organisms in the ICU, Gram positive organisms have remained relatively sensitive to the first line antibiotics so sensitivity in this study is reported with these drugs in mind. The common Gram positive organisms in the ICU include *Coagulase negative Staphylococcus*, *Staphylococcus aureus* and *Group D Streptococcus*.

*Coagulase negative Staphylococcus* is a common skin colonizer and its clinical significance has to be interpreted in each case. *Staphylococcus aureus* has remained relatively sensitive to antibiotics such as amoxicillin-clavulanic acid and cloxacillin. The incidence of resistance to methicillin in the total number of *S aureus* isolates in the hospital in 2004 was 4% and none of these was from the ICU. This represented a decrease from 1994 when it was 9% (16). It is possible that the low level of MRSA in our setting could be due to the absence of epidemic strains of MRSA (EMRSA) but there are no studies documenting this. Resistance to vancomycin in *Staphylococcus aureus* has never been detected at the UHWI.

*Group D Streptococcus* has remained sensitive to ampicillin and amoxicillin-clavulanic acid even though occasional isolates with resistance to vancomycin were identified in the ICU in 2003. Continuous surveillance is necessary to monitor this development. There is a restrictive policy in the hospital that prevents the use of vancomycin without the counter-signature of a Microbiologist resulting in relatively low usage of vancomycin in the hospital. Although this policy is not applicable to the ICU, it contributes to the generally low level of vancomycin resistance in the Gram positive isolates seen in the hospital. *Streptococcus pneumoniae* is not commonly isolated from ICU patients and when it is, it remains sensitive to penicillin and ceftriaxone. A study of the *Streptococcus pneumoniae* isolates at the UHWI (17) showed that only 3.2% of the isolates showed resistance to penicillin compared with 40% in the United States of America (USA). The implications for therapy include the adequacy of empirical penicillin therapy for suspected cases. It must be noted that the link between antibiotic usage and the development of resistance is not necessarily linear as seen by the early emergence of resistance to penicillin in *Staphylococcus aureus* compared with *Streptococcus pneumoniae* where resistance emerged after decades while *Group A Streptococcus* still remains uniformly sensitive to penicillin. However, the fact that there is a link has been borne out by many studies (7) but the emergence of resistance is also influenced by many other factors. Some of these factors include: a) the acquisition of resistance by spontaneous mutation or genetic transfer b) introduction of a resistant organism to a susceptible population c) expression of regulated resistance already present in the population d) selection of a resistant subpopulation and e) dissemination or spread of resistant organisms (1).

It is interesting to note the occurrence of *Stenotrophomonas maltophilia* as the third most common Gram negative isolate overall and the commonest isolate from blood.

The emergence of this isolate as a significant pathogen at the UHWI was first noted in 1997 (3) and since then it has persisted with varying levels of success to control its spread. Its isolation from blood decreases the likelihood of this

organism just being a colonizer. It is also the commonest organism isolated from CVP tips and introduces the possibility of these catheters facilitating the survival and introduction of this organism into the patient. *Stenotrophomonas maltophilia* has been found to be an emerging pathogen in other countries such as the United Kingdom and has been linked to the use of broad spectrum antibiotics. Its emergence has been reported after the use of carbapenems (18) as the organism is intrinsically resistant to this antibiotic and will therefore survive the use of this antibiotic which destroys a broad spectrum of other microbes. At the UHWI the emergence of *S maltophilia* occurred shortly after the carbapenems were introduced into the hospital (3). The success of infection control measures such as barrier nursing, effective surveillance of handwashing policy and technique as well as restricting the use of specific antibiotics such as the carbapenems, in restraining the spread of this organism in this institution (3) underscore the need for ongoing reinforcement of these policies.

*Acinetobacter spp* is a well known nosocomial pathogen. In spite of its ubiquitous nature, it is not known to be highly virulent and although it has been implicated in some very serious infections, it is more often associated with increased morbidity rather than increased mortality. There was a decrease in *Acinetobacter spp* in blood and CVP tips.

*Klebsiella pneumoniae* and *E coli* were not isolated in large numbers from the ICU and when present, were relatively sensitive to the wide range of antibiotics available in the ICU. In the United States of America, data analysed from the National Nosocomial Infections Surveillance System (NNIS) from 1975–2003 showed a decrease in Gram-negative bacteraemia over the period and this was accounted for mainly by a decrease in *E coli* (19). However while numbers decrease, resistance has increased with the emergence of extended spectrum beta-lactamase producing organisms (ESBL's). A study done at the UHWI showed 17% of *K pneumoniae* isolates in 2003 to be ESBL producers with the Paediatric wards accounting for the largest proportion of isolates (20).

Other Gram negative organisms such as *Acinetobacter spp* and *Pseudomonas aeruginosa* are a nosocomial nightmare showing resistance to a wide range of antibiotics such as ciprofloxacin, ceftazidime and *gentamicin* and in some cases they are to be carefully examined as there is significant resistance to this drug in *Acinetobacter spp* and *Pseudomonas aeruginosa*, 97% and 63% respectively, *Acinetobacter spp*, in particular, shows a high level of resistance to most of the antibiotics normally used with a little less than 40% of the isolates being resistant to all the usual antibiotics. *Stenotrophomonas maltophilia* is intrinsically resistant to carbapenems because of the production of chromosomal metallo-beta-lactamases. The drug of choice for this organism is cotrimoxazole along with one or two other antibiotics guided by susceptibility testing. In this study, there was a 20% resistance to cotrimoxazole, a trend that needs close

observation since the organism when it first emerged was almost uniformly sensitive to this antibiotic.

The approach to antibiotic therapy needs to be closely examined as the use of some of the more commonly used antibiotics, such as the third generation cephalosporins, is more commonly associated with the emergence of resistance to other antibiotics, such as the aminoglycosides and quinolones. Antibiotic policies must be implemented and adhered to, in order to prolong the life of the available antibiotics especially those that are active against Gram negative organisms. Many studies have shown that for patients with ventilator associated pneumonia, when the initial empirical antibiotic therapy is inappropriate, the mortality rate is much higher than when antibiotic therapy is appropriate (8–13). This lends urgency to the need to know the prevailing pathogens from various sites and their antibiotic sensitivity patterns so that appropriate empirical therapy can be started initially.

## CONCLUSION

The organisms isolated from the Intensive Care Unit at the University Hospital of the West Indies are similar to those isolated in many ICUs all over the world. Among the Gram negatives, there is a particularly high level of *S maltophilia* and its increasing resistance to the drug of choice for treatment, cotrimoxazole, suggests the need for close monitoring and steps such as antibiotic restriction should be taken to slow this down. *Acinetobacter spp* and *Pseudomonas aeruginosa* pose therapeutic problems because of the resistance shown to many antibiotics.

Gram positive organisms from the ICU at the UHWI remain sensitive to the usual first-line antibiotics such as amoxicillin-clavulanic acid. While it is not possible to prevent the development of antibiotic resistance, it is possible to slow its emergence and eventual spread. The strategies necessary to do this must be understood and implemented in order to preserve the life of the current available antibiotics. These include ongoing surveillance, proper antibiotic stewardship, antibiotic policies, antibiotic restriction, antibiotic cycling, antibiotic combinations and of course, infection control measures(21).

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