

THESIS

NOSOCOMIAL INFECTION RATES IN VETERINARY REFERRAL HOSPITALS:
USING SYNDROMIC SURVEILLANCE TO ESTABLISH BASELINE RATES

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ABSTRACT

NOSOCOMIAL INFECTION RATES IN VETERINARY REFERRAL HOSPITALS: USING SYNDROMIC SURVEILLANCE TO ESTABLISH BASELINE RATES

Nosocomial, or hospital-acquired, infections are considered to be the most common complication affecting hospitalized human patients, but their impact on hospitalized veterinary patients is less well understood. In fact, the incidence of nosocomial infections that occur in veterinary hospitals has not been established. There is evidence, however, that nosocomial infections are of great consequence in veterinary medicine and can have considerable negative effects on the individual patient as well as on the veterinary hospital as a whole. Due to the increased risk of infection in hospitalized patients, it is anticipated that some nosocomial infections will occur. Establishing a baseline rate of infection using surveillance techniques will allow investigators to ascertain the proportion of infections that can be prevented using infection control measures.

The purpose of this study was to establish baseline rates of infection using a syndromic surveillance system created for implementation in small animal and equine referral hospitals. This study included weaned dogs, cats, and horses (n=2248) that were hospitalized in the critical care unit of one of five participating veterinary hospitals during a 12 week period in 2006. Clinicians actively performed syndromic surveillance on hospitalized patients and reported their results no later than the time of the patient's discharge from the hospital.

Adjusted rates of nosocomial events were estimated using Poisson regression, and risk factors associated with an increased risk of developing a nosocomial event were analyzed using multivariable logistic regression.

Adjusting for hospital of admission, 19.7% of horses, 16.3% of dogs, and 12% of cats included in this study were reported to have experienced a nosocomial event occur during hospitalization. The only risk factor found to have a positive association with the development of a nosocomial event in all three species was placement of a urinary catheter. Surgical site inflammation and intravenous catheter site inflammation were two of the most commonly reported events across all species.

Results of this study suggest that nosocomial event rates can be established using syndromic surveillance systems in multiple hospitals. Data pertinent to risk factors for the occurrence of nosocomial events can also be effectively collected using the same technique. Further research is warranted in order to evaluate how generalizable these results are to other veterinary healthcare settings.

DEDICATION

This thesis is dedicated to Dr. Paul Morley who has served many roles for me in the last several years including, but not limited to, being my advisor, mentor, and friend. Without his support and guidance this work would not have been completed.

TABLE OF CONTENTS

1. Review of Literature	1
1.1 Nosocomial Infections: An overview	1
1.2 Nosocomial infection surveillance and control in human healthcare	7
1.2.1 History	7
1.2.2 Staphylococcal epidemics	8
1.2.3 Comprehensive Hospital Infections Project	9
1.2.4 National Nosocomial Infections Surveillance system	10
1.2.5 Study on the Efficacy of Nosocomial Infection Control project	11
1.2.6 Targeted surveillance	15
1.2.7 Rates for interhospital comparison	16
1.2.8 National Healthcare Safety Network	17
1.3 Nosocomial infection surveillance and control in veterinary hospitals ..	19
1.3.1 Surveillance for infection rates associated with a specific outcome	19
1.3.2 Surveillance for specific etiologic agents	23
1.3.3 Environmental Surveillance	25
1.3.4 Infection control programs in veterinary medicine	26
1.4 Establishing the endemic rate of nosocomial infections in veterinary hospitals	28
1.4.1 Standard definitions of infection	29
1.4.2 Determining the population to be included in surveillance	31
1.4.3 Data collection and case finding methods	34
1.4.4 Interhospital data comparison	36
1.5 Conclusions	37
2. Uniform Protocol for Surveillance	38
2.1 Overview	38
2.2 Syndromic surveillance	38
2.2.1 Nosocomial syndrome definitions	39
3. Materials and Methods	41

3.1	Study overview	41
3.2	Case selection.....	41
3.3	Data collection.....	42
3.4	Data analysis.....	44
4.	Results.....	47
4.1	Dogs.....	47
4.1.1	Population characteristics	47
	Table 1. Characteristics of the 1535 dog patients enrolled in the study	48
4.1.2	Occurrence of nosocomial events – Crude Rates.....	49
4.1.3	Occurrence of nosocomial events – Hospital adjusted rates	50
	Table 2. Nosocomial events occurring in dog patients after hospital admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.	50
4.1.4	Risk factors for nosocomial events	50
	Table 3. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of any nosocomial event in dog patients.	52
4.2	Cats.....	52
4.2.1	Population characteristics	52
	Table 4: Characteristics of the 416 cat patients enrolled in the study	53
4.2.2	Occurrence of nosocomial events – Crude Rates.....	54
4.2.3	Occurrence of nosocomial events – Hospital adjusted rates	55
	Table 5. Nosocomial events occurring in cat patients after hospital admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.....	55
4.2.4	Risk factors for nosocomial events	55
	Table 6. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of any nosocomial event in cat patients.	57
4.3	Horses.....	58
4.3.1	Population characteristics	58
	Table 7. Characteristics of the 297 horse patients enrolled in the study.	59
4.3.2	Occurrence of nosocomial events – Crude Rates.....	59

4.3.3	Occurrence of nosocomial events – Hospital adjusted rates	60
	Table 8. Nosocomial events occurring in horses after admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.	61
4.3.4	Risk factors for nosocomial events	61
	Table 9. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of a nosocomial event in horse patients.	63
5.	Discussion and Conclusions	64
6.	References.....	68

1. Review of Literature

1.1 Nosocomial Infections: An overview

Nosocomial, or hospital-acquired, infections are defined by the US Centers for Disease Control and Prevention (CDC) as any localized or systemic condition that occurs in a patient as a result of the presence of an infectious agent or its toxin that was not present or incubating at the time of hospital admission (Horan *et al.*, 2008). Hospitalized patients have an unusually high risk of developing infection due to both intrinsic risk factors, such as underlying disease conditions, and extrinsic risk factors, like the use of invasive devices during hospitalization (National Nosocomial Infections Surveillance System, 1991; Emori & Gaynes, 1993). Hospitalization can further enhance the risk of developing infection by housing patients that have enhanced susceptibility of developing disease in proximity to patients that have a higher likelihood of being infected with infectious agents (Emori & Gaynes, 1993; Morley, 2002). In fact, patients hospitalized within intensive care units have a five to 10 times greater risk of developing a nosocomial infection than other hospitalized patients (Weber *et al.*, 1999).

Nosocomial infections are considered to be the most common complication affecting hospitalized human patients, and hospital-acquired

bloodstream infections are the eighth leading cause of death in the United States (Wenzel & Edmond, 2001; Burke, 2003). Hospital-acquired infections are a significant cause of morbidity and mortality in human healthcare settings, and it is estimated that two million patients are affected each year in the United States resulting in 90,000 deaths, and adding an estimated \$4.5 to \$5.7 billion to the cost of patient care per year (Burke, 2003; Klevens *et al.*, 2007; Atreja *et al.*, 2008). Economic modeling has been used to control for confounding effects, such as severity of illness, in order to determine the true cost of nosocomial infections, and even after controlling for these effects it was estimated that nosocomial infections results in \$15,275 in excess cost per occurrence (Roberts *et al.*, 2003).

Bloodstream infections (BSI) are considered among the most important nosocomial infections in human patients because of the resulting prolongation of hospital stay and increased mortality (Gastmeier *et al.*, 1999). In a case-control study designed to examine the total and attributable mortality of patients with nosocomial BSI, it was determined that nosocomial BSI patients had a 50% mortality compared to 15% in those without BSI, yielding a 35% attributable mortality (Pittet *et al.*, 1994). In the same study it was determined that the excess length of stay attributable to nosocomial BSI was 14 days for all cases and 24 days for affected patients that survived the infection (Pittet *et al.*, 1994). In a prospective study conducted over the course of a year the mortality rate attributed to nosocomial bloodstream infection was estimated to be 28% (Smith *et al.*, 1991). A case-control study conducted in hospitalized neonates found

bloodstream infections to be the most commonly detected nosocomial event and cases were hospitalized an average of 5.2 days longer than controls at a corresponding cost of \$10,440 per infected case (Leroyer *et al.*, 1997).

The incidence of nosocomial infections that occur in veterinary hospitals has not been established (Boerlin *et al.*, 2001; Johnson, 2002; Morley, 2004; Smith, 2004; Traub-Dargatz *et al.*, 2004; Morley & Weese, 2008). We do know, however, that nosocomial infections are of great consequence in veterinary medicine due to several documented nosocomial outbreaks of various etiologies in both large and small animal veterinary hospitals (Castor *et al.*, 1989; Madewell *et al.*, 1995; Hartmann *et al.*, 1996; Konkle *et al.*, 1997; Tillotson *et al.*, 1997; Seguin *et al.*, 1999; Schott *et al.*, 2001; Weese & Armstrong, 2003; Cherry *et al.*, 2004; Ward *et al.*, 2005; Wright *et al.*, 2005; Weese *et al.*, 2006a; Dallap Schaer *et al.*, 2010; Goehring *et al.*, 2010; Steneroden *et al.*, 2010). Duration of these outbreaks was reported to be as long as 13 months (Seguin *et al.*, 1999), multidrug resistance (MDR) was reported in the agents responsible for seven of the outbreaks (Hartmann *et al.*, 1996; Seguin *et al.*, 1999; Schott *et al.*, 2001; Ward *et al.*, 2005; Wright *et al.*, 2005; Weese *et al.*, 2006a; Dallap Schaer *et al.*, 2010), and environmental contamination was detected in 10 of the outbreaks (Castor *et al.*, 1989; Hartmann *et al.*, 1996; Konkle *et al.*, 1997; Tillotson *et al.*, 1997; Schott *et al.*, 2001; Weese & Armstrong, 2003; Ward *et al.*, 2005; Wright *et al.*, 2005; Dallap Schaer *et al.*, 2010; Steneroden *et al.*, 2010). In addition, during six of these outbreaks the affected hospitals were closed in order to mitigate nosocomial spread of disease (Tillotson *et al.*, 1997; Schott *et al.*, 2001; Weese

& Armstrong, 2003; Ward *et al.*, 2005; Dallap Schaer *et al.*, 2010; Goehring *et al.*, 2010), and two hospitals underwent significant facility renovations in order to eradicate environmental contamination (Tillotson *et al.*, 1997; Dallap Schaer *et al.*, 2010). Evidence of zoonotic infection was reported in six of these outbreaks (Konkle *et al.*, 1997; Seguin *et al.*, 1999; Schott *et al.*, 2001; Cherry *et al.*, 2004; Wright *et al.*, 2005; Weese *et al.*, 2006a). In seven of these outbreaks death or euthanasia was reported in animals that had become infected while hospitalized (Hartmann *et al.*, 1996; Konkle *et al.*, 1997; Tillotson *et al.*, 1997; Schott *et al.*, 2001; Dallap Schaer *et al.*, 2010; Goehring *et al.*, 2010; Steneroden *et al.*, 2010). The financial impact due to the nosocomial outbreaks were only estimated in two of the reports. In one case, facility renovations were estimated to cost \$550,000 (Tillotson *et al.*, 1997). In the other case, the outbreak resulted in approximately \$4.12 million of lost revenue due to closure and renovations (Dallap Schaer *et al.*, 2010). Though not directly mentioned in any of these reports, it is important to note that outbreaks of nosocomial infections can tarnish the reputation of a veterinary hospital and may result in decreased client confidence or morale problems among hospital staff. These intangible costs may be at least as significant as the financial losses incurred.

A recent survey of American Veterinary Medical Association (AVMA) accredited veterinary teaching hospitals (Benedict *et al.*, 2008), revealed that 82% (31/38) of hospitals included had identified a nosocomial outbreak in the five years prior to the interview and 45% (17/38) of included hospitals experienced more than one outbreak in the same time period. During the nosocomial

outbreaks, 58% (22/38) of hospitals surveyed had restricted patient admissions in order to diminish spread of disease and 32% (12/38) of hospitals had completely closed sections of the facility in order to control the spread of nosocomial infections (Benedict *et al.*, 2008). Additionally, 50% (19/38) of the institutions included in the study reported significant health problems among hospital personnel attributable to zoonotic infection in the two years prior to the interview (Benedict *et al.*, 2008). Interviewees were not asked to quantify the severity of the reported outbreaks or estimate the financial impact the outbreak(s) had on the institution.

The reports documenting outbreaks of infection suggest that hospital-acquired infections are a concern in veterinary healthcare settings when multiple animals are affected during the same timeframe. However, the acquisition of a nosocomial infection can have potentially severe consequences in the individual animal and are a serious threat to optimum patient care. In fact, it has been shown that nosocomial infection rates can be used as measurement of outcome to reflect quality of patient care in human hospitals (Larson *et al.*, 1988; Raine, 1991; Gaynes, 1997). Nosocomial infections are expected to occur regardless of the precautions taken by an institution, but some nosocomial infections are preventable. Unfortunately, we do not know the proportion of nosocomial infections occurring in veterinary hospitals that are preventable, but it is apparent that the occurrence of nosocomial infections may not be interpreted as unavoidable (Sage, 1998; Morley, 2004; Morley & Weese, 2008). It is therefore necessary for veterinarians to actively manage the risks of nosocomial infections

posed to patients through infection control measures in order to meet the ethical obligations of the profession and provide the best patient care possible (Morley, 2002, 2004; Benedict *et al.*, 2008; Morley & Weese, 2008; Ekiri *et al.*, 2010).

Although many recommendations for nosocomial infection prevention and control have been made as a result of experiences with infectious disease outbreaks (Hartmann *et al.*, 1996; Schott *et al.*, 2001; Wright *et al.*, 2005; Dallap Schaer *et al.*, 2010; Goehring *et al.*, 2010; Steneroden *et al.*, 2010) there are currently no universally recognized published standards or best practices for infection surveillance or control in veterinary healthcare settings. Without implementation of standardized surveillance techniques in veterinary hospitals we will not be able to determine the rates of nosocomial infection or begin to determine the fraction of preventable infections, both of which are necessary in order to guide infection prevention and control efforts and thereby optimize patient care (Morley, 2002, 2004; Benedict *et al.*, 2008; Morley & Weese, 2008).

Formal infection control programs have been used and evaluated in human hospitals for many decades. Many of the factors that have been determined in human healthcare to be contributors to the development of nosocomial infections are becoming increasingly common in veterinary medicine. These include increases in the use of intensive care practices, the use of invasive devices (e.g., intravenous and urinary catheters), prolonged hospitalization of critically ill patients, the performance of complex medical and surgical treatments, and the widespread use of antibiotics (Boerlin *et al.*, 2001; Johnson, 2002). It is therefore important to consider the research data that has

been generated in human hospitals regarding nosocomial infections and control practices, especially since there is generally very little information on these topics in the veterinary literature.

1.2 Nosocomial infection surveillance and control in human healthcare

1.2.1 History

One of the earliest studies of hospital epidemiology was conducted at the University of Edinburgh by Sir James Young Simpson in 1869. Simpson collected data on more than 4000 amputees by surveying surgeons throughout Scotland and England. Information obtained from the surgeons included how many amputations they had performed, the type of amputation performed, where the patient had recovered from surgery, and whether the patient had lived or died. Simpson found the mortality rate to be higher in patients who remained in the hospital post-operatively. Simpson (1869) used the term “hospitalism” to describe the increased risk related to hospital care he observed during his study.

It took many decades of work by some of the founders of modern bacteriology and the germ theory of disease, such as Oliver Wendell Holmes, Ignaz Philipp Semmelweis, Louis Pasteur, Joseph Lister, and Robert Koch, to elucidate some of the risk factors that were associated with hospital-related infections (Semmelweis, 1848; Major, 1954; Eickhoff, 1981). The introduction of basic infection control principles such as hand washing and sterilization of surgical instruments decreased the spread of disease and reduced mortality rates for patients (Major, 1954). The discovery of antibiotics resulted in what has

been termed a “tide of complacency” in the history of hospital infection control, because the study of nosocomial infections was not advanced a great degree in the period of time between the world wars (Eickhoff, 1981).

1.2.2 Staphylococcal epidemics

Nosocomial infections did not become a major topic of study in the US again until the late 1950s when a nationwide epidemic of hospital-based staphylococcal infections was recognized as a crucial public health issue (Anderson, 1958; Haley *et al.*, 1980b; Burke, 2003). The US CDC and the National Academy of Sciences hosted a national conference about the staphylococcal epidemic in 1958 with the primary objective being to develop a nationwide program for the control of hospital-acquired staphylococcal disease (Anderson, 1958). Delegates were in attendance from all major medical organizations within the US, including the American Veterinary Medical Association (AVMA). At the conclusion of the conference, it was unanimously agreed that the establishment of hospital infection control committees was necessary and the primary responsibilities of those committees should include surveillance for infections, infection control, and education of hospital personnel (“Summary Report,” 1958). Based upon these proceedings the American Hospital Association (1958) published a recommendation that all hospitals establish “committees on infection,” which was one of the first major endorsements for infection control committees in hospitals. One of the biggest challenges for these infection control committees was the development of a surveillance system that could be used to detect nosocomial infections because,

as stated by Dowling (1958), “infections cannot be controlled unless we know they are there.”

The estimation of rates of nosocomial infection in the US began with surveillance studies conducted in individual hospitals. The first of these studies determined the prevalence of nosocomial infections and were conducted at Boston City Hospital in 1964 (Kislak *et al.*) and 1967 (Barrett *et al.*, 1968). These studies looked for infection at all sites among all hospitalized patients and reported the combined, or overall, infection rate (Kislak *et al.*, 1964; Barrett *et al.*, 1968). Next, a pilot surveillance project was conducted in six hospitals in collaboration with the CDC in 1965 and 1966 (Eickhoff *et al.*, 1969). The methods of surveillance employed varied somewhat among the hospitals, but similarities included the use of an infection report form that was filled out by doctors or nurses in direct contact with patients and a designated surveillance nurse who was responsible for recording the number and types of infections reported (Eickhoff *et al.*, 1969). The definition of nosocomial infection used in these studies was a clinical infection that developed at any time during hospitalization. This definition was broad and diagnosis of infection was based primarily on clinical judgment as laboratory confirmation of the presence of an infectious agent was not required for a nosocomial infection to be reported (Eickhoff *et al.*, 1969).

1.2.3 Comprehensive Hospital Infections Project

The first systematic effort to estimate the rate of nosocomial infection was the Comprehensive Hospital Infections Project (CHIP), which was conducted by the CDC between 1969 and 1973 and involved active surveillance for nosocomial infections in eight hospitals (Bennett *et al.*, 1970; Scheckler & Bennett, 1970; Stamm *et al.*, 1977). Surveillance in this project was used to detect nosocomial infections at all sites within the entire hospital population, termed hospital-wide total surveillance (Hughes, 1987). One of the most important outcomes of the CHIP studies was the development of uniform definitions for nosocomial infections and development of uniform surveillance methods for detection of nosocomial infections in community hospitals (CDC, 1997).

1.2.4 National Nosocomial Infections Surveillance system

As a result of these initial investigations, in 1970 the CDC recommended that all hospitals establish positions for a hospital epidemiologist and infection control nurse (Hughes, 1987). In the same year the CDC also began operation of the National Nosocomial Infections Study, later renamed the National Nosocomial Infections Surveillance (NNIS) system (Emori *et al.*, 1991). The NNIS was able to accept data regarding nosocomial infections from up to 80 hospitals nationwide (CDC, 1997). The voluntary contributors to the system agreed to conduct active hospital-wide surveillance, monitoring all patients who stayed at least overnight for uniformly defined nosocomial infections at all sites, and report only infections that occurred during hospitalization or shortly after discharge that were not present or incubating at the time of the patient's admission (Horan *et al.*, 1986; Hughes, 1987; Emori *et al.*, 1991). The CDC

used the data collected through this system to calculate the overall nosocomial infection rate in US hospitals (Horan *et al.*, 1986). In 1976, the Joint Commission on the Accreditation of Hospitals established requirements regarding nosocomial infection surveillance and strongly recommended the use of dedicated surveillance personnel (Hughes, 1987). Most surveillance activities in this time period were directed towards infections within patients, but many hospitals employed extensive routine environmental culturing for infectious agents as part of their infection control program (Haley & Shachtman, 1980).

1.2.5 Study on the Efficacy of Nosocomial Infection Control project

Despite the growing popularity of surveillance and infection control programs there was little data to support their efficacy in reducing the occurrence of nosocomial infections (Britt *et al.*, 1978; Eickhoff, 1978, 1980; Sharbaugh, 1981). In order to evaluate the effectiveness of hospital infection prevention and control programs the CDC launched a series of national epidemiologic studies between 1974 and 1983, known collectively as the SENIC project (Eickhoff, 1980; Emori *et al.*, 1980; Haley *et al.*, 1980a, 1980b; Haley and Shachtman, 1980; Quade *et al.*, 1980; Eickhoff, 1981; Haley *et al.*, 1985a, 1985b, 1985c; Hughes, 1987; Haley, 1995). This was a major undertaking and the first results from this project were not published until 1980, when the American Journal of Epidemiology devoted an entire issue to the methods section alone (Eickhoff, 1981). The overarching hypothesis studied in SENIC was that in order to reduce the nosocomial infection rates an infection control program must have four components: surveillance, control (e.g., disinfection), a dedicated infection

control officer (infection control nurse), and a physician or microbiologist with special skills in infection control actively involved in the infection control program (Haley *et al.*, 1980b). The initial study design was an observational study conducted in three phases. In the first phase the investigators used a screening questionnaire to measure the extent to which more than 6000 hospitals had already implemented each of the components outlined in the hypothesis (Haley *et al.*, 1980b). A sample of 338 hospitals was randomly selected from those participants in the first phase for enrollment in the second and third phases of the study, which consisted of on-site interviews to determine the exact nature of each hospital's infection control program and measure the nosocomial infection rates in each hospital in the year before each started the infection control program and five years later (Haley *et al.*, 1980b). The latter phases utilized a retrospective chart review process that was determined to have an average sensitivity of 0.74 and an average specificity of 0.96 (Haley *et al.*, 1980a).

The results of this study showed there were three essential components to effective infection control programs: surveillance, control, and feedback of nosocomial infection rates to hospital personnel (Haley *et al.*, 1985a). In those hospitals that had all three essential components present, the addition of the involvement of a physician or microbiologist with special skills in infection control further reduced the overall rate of nosocomial infection; conversely, if any of the three essential components were missing from the infection control program no reduction was observed in the nosocomial infection rate (Haley *et al.*, 1985a). In fact, the overall infection rate was reduced by 32% in hospitals that implemented

all four components of the infection control program and the rate of nosocomial infection actually increased among hospitals that did not establish prevention programs (Haley *et al.*, 1985a). Infection rates at four specific sites (surgical-site infection, pneumonia, urinary tract infection, and bacteremia) were also examined and different combinations of the infection control practices reduced infections at each site, but surveillance was the only component essential for reduction of nosocomial infection rates at all four sites (Haley *et al.*, 1985a).

The final phase of the SENIC project involved resending the survey used in the first phase of the initial study to 444 randomly selected hospitals throughout the US in 1983 (Haley *et al.*, 1985b). The data was analyzed to estimate the frequency of characteristics and activities at each time point and assess the directions and types of changes in individual hospitals. The results of this study showed the overall intensity of surveillance and infection control programs had increased substantially and there was therefore an increase in the number of nosocomial infections being prevented by these programs (Haley *et al.*, 1985b). An additional financial analysis was conducted and it was concluded that an effective infection surveillance and control program could substantially reduce hospitalization costs (Haley *et al.*, 1985b). However, the overall cost of the infection control program was not factored into the analysis done for this part of the study. Interestingly, the practice of routine environmental culturing for infectious agents, once considered an integral part of infection control programs, was rarely found to be used within the hospitals surveyed (Haley *et al.*, 1985b).

The results of the SENIC project established the scientific basis for the use of surveillance in reducing the rate of nosocomial infections, but they also revealed the need for refinement of the surveillance methods and control efforts being used by hospitals. Even though there had been a great increase in the amount of effort being expended by hospitals to reduce nosocomial infection rates between 1976 and 1983, there was only a slight improvement in the level of effectiveness of infection control as measured by the SENIC project (Haley *et al.*, 1985b). The SENIC data showed that only a few of the hospitals surveyed had efficient infection control programs, defined as having a linear relationship between effort expended and reduction in nosocomial infection rates, in place. The authors suggested that the lack of efficient programs may have been due to the uncertainty about the effectiveness of specific preventive approaches (Haley *et al.*, 1985b). Additionally, even those hospitals that had implemented efficient infection control programs were not operating at a maximal level of effectiveness (the level of effort expended did not result in an adequate decrease in the rate of nosocomial infections). These infection control programs that were deemed to be efficient by the SENIC investigators had been able to reduce nosocomial infection rates at one or more specific sites, but virtually none of these programs had implemented all of the components necessary to reduce infection rates at all sites at the same time (Haley *et al.*, 1985a, 1985b). In the final report of the results of the SENIC project the authors concluded that surveillance was an essential activity for effective infection control programs, but additional studies

were needed to determine more efficient approaches to conducting surveillance (Haley *et al.*, 1985a).

1.2.6 Targeted surveillance

In 1985 a more refined approach to nosocomial infection surveillance strategies was proposed, primarily due to the results of the SENIC study that showed that different control activities were effective at preventing infections at different sites (Haley, 1985). Termed “surveillance by objective,” the concept was a type of targeted surveillance that eliminated the collection of data regarding overall hospital infection rates and suggested hospital infection control personnel collect data regarding nosocomial rates that were either site specific (e.g., surgical site infection) or unit-directed (e.g., intensive care unit) (Haley, 1985). In this scheme, the infection control personnel determined the most serious nosocomial infection problems at each hospital and developed a specific control strategy targeted at reducing the rates of nosocomial infection that were of greatest consequence to their units (Haley, 1985). Over the next decade most hospitals in the US changed their surveillance programs to more closely align with this concept of objective-oriented or targeted surveillance (Haley, 1995). This change was reflected in the NNIS system by the addition of three surveillance components, which were introduced in 1986, that allowed hospitals to meet their own targeted surveillance objectives while still providing data to the national surveillance effort (Hughes, 1987; NNIS, 1991). In addition to the collection of hospital-wide surveillance data the NNIS also began collecting data

about adult and pediatric intensive care unit surveillance, high-risk nursery surveillance, and surgical patient surveillance (NNIS, 1991).

1.2.7 Rates for interhospital comparison

Though the NNIS did continue to collect data regarding the crude hospital-wide nosocomial infection rate, limitations for its utility as a basis for interhospital comparison were increasingly recognized (Haley, 1985; Fuchs, 1987). One such limitation is that most of the data collected in hospital-wide surveillance is from infected patients (numerator data) and is a combination of infections from all sites (Emori *et al.*, 1991; NNIS, 1991). Using the rates determined by a single overall infection rate for interhospital comparison does not take into account that risk factors contributing to the development of infection differ for each site of infection. Additionally, the data collected on the population at risk of becoming infected (denominator data) reflects the overall number of patients discharged from the hospital and is therefore not able to measure the influence of exposure to risk factors for nosocomial infections, such as catheterization or surgery (Emori *et al.*, 1991). The additional surveillance components used by the NNIS were designed to overcome this by including patients who were exposed to a common extrinsic risk factor in the numerator and the number of exposures to that risk factor in the denominator (Emori *et al.*, 1991; NNIS, 1991). A second limitation of use of the overall infection rate for interhospital comparison is the lack of measurement of intrinsic patient risk (Hughes, 1987). The NNIS surveillance components introduced in 1986 addressed this deficiency by focusing on collecting data on groups of patients that were considered to be at high risk of infection and

including a patient risk index in order to adjust rates of nosocomial infection based on intrinsic risk factors (e.g., severity of underlying illness, length of hospitalization, and exposure to invasive devices and procedures) (Emori *et al.*, 1991; NNIS, 1991). These risk-specific rates are then used for interhospital comparison and for individual hospitals to set priorities for their infection control programs (Emori *et al.*, 1991).

Another improvement to the NNIS system was that the CDC developed a new set of standard definitions for surveillance of nosocomial infections in 1988 (Garner *et al.*, 1988). The definitions combined clinical findings with results of laboratory and other tests and were formulated as algorithms (Garner *et al.*, 1988). In addition to definitions for common nosocomial infections there was also inclusion of definitions of infrequently diagnosed infections that have severe consequences (Garner *et al.*, 1988). This standardized approach to defining the occurrence of nosocomial infections was necessary for hospitals to accurately compare rates of nosocomial events. In fact, these new guidelines allowed implementation of the NNIS-type surveillance in hospitals in other countries and the techniques employed in the acquisition of nosocomial infection rates were so standardized that it allowed for comparison of infection rates internationally (Ferguson & Gill, 1996).

1.2.8 National Healthcare Safety Network

In 2004 the NNIS system was combined with two other CDC-conducted national surveillance systems into a single internet-based system, the National

Healthcare Safety Network (NHSN), which is still in use today (Tokars *et al.*, 2004). A few major changes in the national surveillance effort occurred when these systems were combined, but arguably the biggest change was that there was a shift from tracking the occurrence of all infections to only tracking infections that occurred in association with invasive devices or the occurrence of post-procedure pneumonia or surgical site infection (Tokars *et al.*, 2004). The NHSN also expanded surveillance beyond intensive care units and included the collection of data on outpatient surgery (Tokars *et al.*, 2004).

Today the patient safety component of the NHSN system, the component most analogous to the NNIS, has three modules: the device-associated module (for infections associated with invasive devices), the procedure-associated module (for post-procedure infections), and the medication-associated module (for antimicrobial use and susceptibility) (Edwards *et al.*, 2009). Most of these modules require active, patient-based, prospective surveillance by a trained member of the hospital infection control program (CDC, 2010). The NHSN system can upload data directly from participating hospital's databases and automatically calculate the risk-adjusted rate of nosocomial infections. This allows interhospital comparisons to be made easily and eliminates the possibility of differences in nosocomial rates resulting from variations in calculation methods (Edwards *et al.*, 2009). In addition to providing national rates of nosocomial infections for interhospital comparisons, the NHSN links data submitted for surveillance purposes to online prevention tools (guidelines and workbooks) and generates automatic email alerts for selected adverse events (Edwards *et al.*,

2009). The methods used by the NHSN surveillance system are nationally and internationally recognized as the standard for hospital-associated infection surveillance (Daschner *et al.*, 2004; CDC, 2008; Rosenthal *et al.*, 2010).

1.3 Nosocomial infection surveillance and control in veterinary hospitals

Studies conducted in veterinary hospitals to determine the rate of nosocomial infection are extremely limited compared to those performed in human hospitals. Most published data from veterinary hospitals is limited to either a single outcome (e.g., surgical site infection) or a specific etiologic agent (e.g., *Staphylococcus aureus*). Also, studies are typically restricted to one species and evaluate only one procedure type (e.g., orthopedic surgery). Although prior reports do not establish the overall incidence of nosocomial infections in veterinary hospitals, they do document that nosocomial infections occur on a regular basis and suggest that this type of infection is a serious problem in veterinary medicine.

1.3.1 Surveillance for infection rates associated with a specific outcome

An example of a specific nosocomial outcome that has been reported in the veterinary literature is urinary tract infection. Most of the published studies examining this outcome are restricted to dogs that had a urinary catheter placed during hospitalization (Wise *et al.*, 1990). In a prospective study reported by Biertuempfel and others (1981), 20% of healthy female dogs developed bacteriuria after a single catheterization of the urinary bladder. All of these dogs had a urine specimen collected prior to catheterization and no bacteria were

isolated from these samples (Biertuempfel *et al.*, 1981). Another prospective study (Smarick *et al.*, 2004) that included dogs with no bacterial growth in urine collected prior to catheterization found that 10.3% of catheterized dogs developed a urinary tract infection. This study (Smarick *et al.*, 2004) may have resulted in a smaller proportion of affected dogs because it included more male than female dogs, and it has been shown that female dogs are at greater risk of developing urinary tract infections than are male dogs (Biertuempfel *et al.*, 1981). Bubenik and Hosgood (2008) reported a randomized clinical trial that included dogs that had undergone surgery to repair intervertebral disk disease. Dogs were stratified based on sex and then randomly assigned to one of three bladder management treatments: manual expression, indwelling catheterization, or intermittent catheterization (Bubenik & Hosgood, 2008). The group of dogs with indwelling catheters had the highest proportion of urinary tract infection, with 32% of dogs showing detectable growth of at least one bacterial species post-catheterization (Bubenik & Hosgood, 2008).

Infections associated with intravenous catheterization are thought to be one of the top two causes of nosocomial infections in animals (Marsh-Ng, Burney, Garcia, 2007) and most of these types of infection are caused by contamination of the intravenous device (Johnson, 2002). Several studies have been conducted to determine the prevalence of intravenous catheter contamination in small animal hospitals. In one such study, catheters from all dogs and cats admitted to the intensive care unit at Ontario Veterinary College during a one year period were cultured for bacterial contamination and the overall

contamination rate was 10.7% (Mathews, Brooks, & Valliant, 1996). Another study that evaluated the rate of bacterial contamination of intravenous catheters collected from 100 dogs found the contamination rate to be 22%, with most bacteria isolated being of gastrointestinal tract or environmental origin (Lobetti, Joubert, Picard, Carstens, & Pretorius, 2002). Other similar studies have reported bacterial contamination rates of intravenous catheters recovered from dogs and cats to be 24.5% (Marsh-Ng *et al.*, 2007) and 23.2% (Jones, Case, Stevens, Boag, & Rycroft, 2009).

Surgical site infection rates have also been determined in a few veterinary studies. The National Research Council's operative wound classification system was utilized in some of the studies used to determine surgical site infection rates (Vasseur *et al.*, 1988; MacDonald *et al.*, 1994; Nicholson *et al.*, 2002). This classification system is based upon the level of intrinsic microbial contamination present at the time of surgery and the categories included are clean, clean-contaminated, contaminated, and dirty (Adam & Southwood, 2006). Although the number of surgical site infections is expected to be higher in wounds with a greater degree of contamination, this increase in rate is not strictly proportional (Adam & Southwood, 2006). A study of equine surgical patients with clean or clean-contaminated wounds at a veterinary teaching hospital determined the overall rate of surgical site infection to be 10%, but the infection rate in patients with wounds classified only as clean-contaminated was 52.6% (MacDonald *et al.*, 1994). A more recent study examined post-operative orthopedic infections in horses and determined the overall rate of nosocomial infection to be 28% (Ahern

et al., 2010). The standards used to define a wound as infected were different for these studies, which likely accounts for some of the discrepancy between the reported infection rates. A retrospective study of surgical wound infections in dogs and cats found the overall rate of infection to be 5.1%, with the lowest proportion of infections (2.5%) occurring in animals with surgical wounds classified as clean and the highest proportion of infections (18.1%) having occurred in animals with wounds classified as dirty (Vasseur *et al.*, 1988). Another retrospective study included only infections in clean-contaminated surgical wounds of dogs and cats and determined the rate of infection to be 5.9% (Nicholson *et al.*, 2002). A subsequent prospective study in dogs and cats found the surgical site infection and inflammation rate to be 8.8%, but this study did not stratify patients based upon the operative wound classification system (Eugster *et al.*, 2004). All of the studies in small animal patients used clinical evidence as the basis for a diagnosis of surgical site infection, but a uniform definition was not used by all of these studies. Only one of these studies (Nicholson *et al.*, 2002) collected information regarding the occurrence of surgical site infection after the animal was discharged from the hospital and that information was only collected at the time of suture removal. In human studies it has been shown that approximately half of surgical site infections become evident after the patient is discharged (Burns & Dippe, 1982; Brown *et al.*, 1987; Reimer *et al.*, 1987; Law *et al.*, 1990; Delgado-Rodriguez *et al.*, 2001) and infections of surgical wounds classified as clean or clean-contaminated were actually more likely to be diagnosed after hospital discharge (Brown *et al.*, 1987; Delgado-Rodriguez *et al.*,

2001). If these findings were to hold true in veterinary medicine then it is likely that the rate of surgical site infection is grossly underreported.

1.3.2 Surveillance for specific etiologic agents

In some institutions surveillance is performed for specific etiologic agents that are known to cause nosocomial infection. In the survey conducted by Benedict *et al.* (2008) 53% of hospitals reported that collection of samples from patients for detection of specific contagious pathogens was part of their infection control practice. One such agent that is often included in hospital surveillance programs is *Salmonella*, an agent that is commonly reported in association with veterinary nosocomial outbreaks in both large and small animal patients (Schott *et al.*, 2001; Cherry *et al.*, 2004; Benedict *et al.*, 2008; Steneroden *et al.*, 2010). Surveillance is often restricted to patients known to be at high risk of shedding *Salmonella* (Morley, 2002, 2004; Morley & Weese, 2008; Ekiri *et al.*, 2010). Sampling may involve collection of a fecal sample from each patient at the time of admission and then at regular intervals during hospitalization (Morley, 2002; Ekiri *et al.*, 2010). In general, salmonellosis is considered to be of nosocomial origin if *Salmonella* was not detected in the original patient sample, but was isolated from a subsequent sample obtained after at least 72 hours of hospitalization, and the organism has the same serotype and antimicrobial resistance pattern as other isolates detected in the patient population (Ekiri *et al.*, 2010). In a study reported by Kim and others (2001) surveillance for *Salmonella* in fecal samples collected from 246 horses hospitalized for colic resulted in

detection of *Salmonella* organisms in at least one fecal sample from nine percent of the study population.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is considered the most important nosocomial pathogen in human medicine and is probably one of the best described emerging multiple drug resistant bacteria in veterinary medicine (Beard, 2010). A survey of *S. aureus* isolates recovered from veterinary patients treated at seven teaching hospitals in the United States determined that 14% of patients were infected with MRSA, with the highest prevalence of MRSA infection occurring in dogs and horses (Middleton *et al.*, 2005). In order to determine the prevalence of MRSA in equine patients at the Ontario Veterinary College a screening program was instituted in which samples were collected on all horses at the time of admission to the hospital, weekly during hospitalization, and at the time the patient was discharged from the hospital (Weese *et al.*, 2006b). MRSA was isolated from 5.3% of horses admitted to the hospital during the 20-month study period, but 50.8% of those positive cultures were detected at the time of admission to the veterinary hospital (Weese *et al.*, 2006b). A study that collected samples on a single day from 45 dogs and 12 cats hospitalized in a small animal referral hospital found the prevalence of MRSA in the canine population to be 9% (Loeffler *et al.*, 2005). There have also been reports documenting an apparent increase in the number of MRSA infections in companion animals, with the majority of those infections occurring at surgical sites (Boag *et al.*, 2004; O'Mahony *et al.*, 2005).

1.3.3 Environmental Surveillance

Surveillance for specific agents in veterinary hospitals may also be conducted through environmental surveillance. In the survey conducted by Benedict and others (2008) 74% of hospitals reported they routinely submitted environmental samples for bacterial culture. Environmental persistence of nosocomial pathogens has been shown to be a problem in human hospitals and many different fomites have been identified as reservoirs of nosocomial organisms, such as stethoscopes (Nunez *et al.*, 2000), endoscopes (Schelenz & French, 2000; Cowen, 2001), computer keyboards (Bures *et al.*, 2000), and thermometers (Van den Berg *et al.*, 2000). Similar studies performed in veterinary hospitals have shown contamination of multiple-dose vials (Sabino & Weese, 2006) and sponge pots containing benzalkonium chloride (Fox *et al.*, 1981), a biocide used prior to intravenous catheter placement.

Additionally, environmental contamination in veterinary hospitals has been shown to have contributed to the occurrence of outbreaks of nosocomial infections (Castor *et al.*, 1989; Hartmann *et al.*, 1996; Tillotson *et al.*, 1997; Schott *et al.*, 2001; Weese & Armstrong, 2003; Ward *et al.*, 2005; Wright *et al.*, 2005; Dallap Schaer *et al.*, 2010; Steneroden *et al.*, 2010) and agents responsible for these outbreaks can be found more commonly in the environment when nosocomial rates are elevated (Burgess *et al.*, 2004). Environmental surveys for the presence of *Salmonella* spp. have resulted in the detection of *Salmonella* in as few as 2.1% (Alinovi *et al.*, 2003) of samples obtained and as many as 11.9% (Burgess *et al.*, 2004) of samples, though collection procedures

were not standardized. An environmental survey for the presence of *Clostridium difficile* in a veterinary teaching hospital detected its presence in 6.3% of samples obtained (Weese *et al.*, 2000). A similar survey detected MRSA in 9.6% of sites sampled throughout the hospital (Weese *et al.*, 2004). In an evaluation of the Royal Veterinary College hospital environment for contamination by staphylococci, 55.9% of samples obtained had a staphylococcal count ≥ 2.5 cfu/cm², the maximum hygiene standard recommended for human institutions in the United Kingdom (Aksoy *et al.*, 2010).

1.3.4 Infection control programs in veterinary medicine

Infection control, or biosecurity, programs are considered to be an integral part of the successful operation of any veterinary practice (Morley, 2002; Traub-Dargatz *et al.*, 2004; Benedict *et al.*, 2008; Morley & Weese, 2008), but there are currently no national standards for infection control programs in veterinary healthcare settings. Through the accreditation process, the AVMA insures that veterinary teaching hospitals have an infection control plan that is “appropriate for caseload” and they require evidence of program effectiveness, specifically stating that “nosocomial infection rate, results, and analysis of microbial surveillance” should be available (AVMA, 2010). They do not, however, provide any guidelines for the institution of infection control programs nor do they have any recommendations on data collection for the purpose of demonstrating program efficacy. The survey conducted by Benedict and others (2008) gives some insight into the structure of existing infection control programs at AVMA accredited veterinary teaching hospitals. Results of that survey showed infection

control programs at most institutions were overseen by an infection control committee and usually one person was responsible for leading infection control activities (Benedict *et al.*, 2008). Most institutions also have written policy documents concerning the infection control program (Benedict *et al.*, 2008). There was less consistency among institutions with respect to microbial surveillance, with only 53% of hospitals collecting samples from patients for detection of specific pathogens and only 58% of institutions compiling information about the occurrence of specific diseases or disease syndromes (Benedict *et al.*, 2008). Very few hospitals collected data regarding the occurrence of disease at predefined temporal intervals (Benedict *et al.*, 2008).

The lack of standardization in veterinary infection control programs may be due in part to the fact that most published recommendations for establishment of programs in veterinary hospitals have not promoted the idea of a standardized approach to infection control, but have rather suggested that programs be customized for each institution (Morley, 2002; Traub-Dargatz *et al.*, 2004; Morley & Weese, 2008). Also, most of the data published in the veterinary literature regarding effectiveness of infection control programs focuses on hygiene protocols (Dunowska *et al.*, 2006) and disinfection of the hospital environment (Dunowska *et al.*, 2005; Patterson *et al.*, 2005). There has been little objective data published on the effects of other infection control measures (Morley, 2004; Murphy *et al.*, 2010), and the topic of infection control is relatively new to veterinary medicine.

One of the biggest hurdles to development of infection control programs in veterinary institutions is that the baseline rate of endemic infection in the veterinary hospital setting has not been established (Boerlin *et al.*, 2001; Johnson, 2002; Morley, 2004; Smith, 2004; Traub-Dargatz *et al.*, 2004; Morley & Weese, 2008). Some fraction of the nosocomial infections that occur in veterinary hospitals are simply not preventable, given the intrinsic and extrinsic risk factors present in both the patient and hospital environment (Eickhoff, 1981; Brachman, 1993; Morley, 2004; Morley & Weese, 2008). This endemic rate of nosocomial infection must be identified in order to target prevention efforts to the preventable fraction of nosocomial infections and determine alterable risk factors for the development of nosocomial infections (Burke, 2003; Morley, 2004; Morley & Weese, 2008). The only way to determine the endemic rate of nosocomial infection or to determine an acceptable rate of infection is through surveillance for nosocomial infections (Burke, 2003; Morley, 2004; Morley & Weese, 2008). Once the endemic rate of nosocomial infection in veterinary hospitals is established it will be easier to evaluate efforts made to prevent their occurrence and it can therefore be determined which infection control strategies should be part of veterinary infection control programs (Burke, 2003).

1.4 Establishing the endemic rate of nosocomial infections in veterinary hospitals

There is no set standard for surveillance for nosocomial infections in veterinary hospitals, therefore a uniform protocol must be developed in order to determine the endemic rate of infections in veterinary healthcare settings. The

definitions used to identify an infection, the methods used to detect infections, and the population of hospitalized patients that are monitored must be consistent in order for determined rates to be meaningful for comparisons either within a hospital over time or between hospitals (Garner *et al.*, 1988; Gaynes, 1997; Pottinger *et al.*, 1997). It is imperative to use the literature available in both the human and the veterinary medical fields in order to design such a surveillance system.

1.4.1 Standard definitions of infection

Unfortunately, nosocomial infections cannot be easily defined. Defining infections in veterinary populations might even be more difficult than in human populations because in order for rates to be comparable between different hospital services the definition of a nosocomial infection must be applicable to multiple species. Many of the definitions used in human hospitals include laboratory based definitions of infection (Emori & Gaynes, 1993; Alberti *et al.*, 2002; Peterson & Brossette, 2002; Brossette *et al.*, 2006). Some research pertaining to nosocomial infections in veterinary medicine have also included laboratory confirmation of infection (Biertuempfel *et al.*, 1981; Mathews *et al.*, 1996; Lobetti *et al.*, 2002; Smarick *et al.*, 2004; Marsh-Ng *et al.*, 2007; Bubenik & Hosgood, 2008; Jones *et al.*, 2009), but other studies have not included laboratory confirmation (Vasseur *et al.*, 1988; MacDonald *et al.*, 1994; Nicholson *et al.*, 2002; Eugster *et al.*, 2004; Ahern *et al.*, 2010). Though laboratory based diagnoses are very specific, their use in veterinary infection surveillance may be limited in part due to the cost of diagnostic laboratory submissions. An additional

reason that laboratory based definitions might be avoided is due to the time required for laboratory confirmation of infection. In situations where an outbreak is suspected, waiting for laboratory diagnosis of disease could significantly hinder the speed of response by the infection control team.

Another way to define nosocomial infections is through clinical definitions of disease. These definitions can be simple indicators of any adverse event (e.g., fever of undetermined origin) or they can be grouped into well-defined patterns of signs and symptoms of disease (Mostashari & Hartman, 2003). This type of surveillance, termed syndromic surveillance, has gained much attention in the human medical field over the last decade because of its potential use as an early warning system in outbreak surveillance related to bioterrorism (Lombardo *et al.*, 2003). In the human medical field, syndromic surveillance can be used to monitor non-clinical data, such as school absenteeism or sales of over-the-counter medications, or clinical data sets, such as flu-like symptoms (Buckeridge *et al.*, 2003; Lombardo *et al.*, 2003; Mostashari & Hartman, 2003). Because most of the biological agents deemed to be high-priority with respect to bioterrorism potential by the CDC are also zoonotic, it has been recommended that syndromic surveillance systems for companion animals be instituted nationwide (Stone & Hautala, 2008). Two such programs currently under development are the National Companion Animal Surveillance Program (NCASP) and the Rapid Syndrome Validation Project-Animal (RSVP-A) (Burns, 2006; Glickman *et al.*, 2006; Vourc'h *et al.*, 2006). It was noted, however, that the use of syndromic surveillance in veterinary populations could simultaneously

be used to provide information regarding disease incidence, prevalence, and risk factors for development of disease in order to aid in the development of evidence-based veterinary practices (Stone & Hautala, 2008). Syndromic definitions have been used in veterinary hospitals for surveillance for surgical-site infections; however the definitions used have varied between studies (Vasseur *et al.*, 1988; MacDonald *et al.*, 1994; Nicholson *et al.*, 2002; Eugster *et al.*, 2004; Ahern *et al.*, 2010).

The benefits of using syndromic surveillance systems for detection of nosocomial infections include the rapidity of detection, the ability to apply the system in a multitude of settings, and the potential for a lower cost system than one that is based upon laboratory diagnosis. Additionally, though the specificity of syndromic surveillance may be relatively low, the sensitivity of system can be increased by ensuring the definitions used for disease syndromes include relevant markers of disease (Van Metre *et al.*, 2009) and by focusing on limited risk factors for development of nosocomial infection (i.e., device-associated infections) (Gastmeier *et al.*, 2000). The eventual goal for defining nosocomial events in veterinary hospitals will likely combine the clinical appearance of disease with laboratory confirmation, much like the definitions of nosocomial events used in the NHSN surveillance system (Tokars, 2004; Edwards, 2009).

1.4.2 Determining the population to be included in surveillance

Hospital-wide surveillance is still used in limited situations in human healthcare settings, such as in acute-care hospitals (Mintjes-de Groot *et al.*,

2000). These systems are very costly and they tend to identify a larger portion of infections that cannot be prevented (Pottinger *et al.*, 1997). Hospital-wide surveillance can also be labor intensive and time consuming to perform, which has led to several studies being conducted with the specific intent of developing a surveillance system that increases the efficiency of surveillance efforts. One such study evaluated the trends in nosocomial infections in the University of Virginia Hospital over an eight year period (Landry *et al.*, 1982). In this study it was determined that the rate of nosocomial infections was nearly four times greater in the critical care areas of the hospital than in the general medicine and surgery wards (Landry *et al.*, 1982). Additionally, there were seven outbreaks of infectious disease during the time period included in the study, and all seven of them involved either exclusively or primarily patients in the critical care areas of the hospital (Landry *et al.*, 1982). Another study performed at the same hospital determined that the efficiency of surveillance systems for detection of nosocomial infection was greatest when focused on patients hospitalized in intensive care units (Wenzel *et al.*, 1981). In a study performed in an intensive care unit in a hospital in Germany researchers found there was only a small decrease in sensitivity and specificity when targeting surveillance to the more narrow population when compared to monitoring the entire hospital population (Dettenkofer *et al.*, 2001). A separate study found that by selecting patients considered to be at an increased risk of developing nosocomial infections the surveillance process took less time, cost less money, and that by decreasing the

number of patients screened actually increased the sensitivity of the detection system (Brusaferro *et al.*, 2006).

The use of a targeted approach to surveillance in veterinary hospitals is very common and global surveillance is typically considered an inefficient use of resources (Morley, 2004). Surveillance for device-associated infections in small animal patients is almost exclusively performed using the patient population hospitalized in the intensive care unit (Mathews *et al.*, 1996; Lobetti *et al.*, 2002; Smarick *et al.*, 2004; Marsh-Ng *et al.*, 2007; Bubenik & Hosgood, 2008). Surveillance for specific etiologic agents, such as *Salmonella*, in equine patients is typically performed on those patients housed in the colic ward or other intensive care area of the large animal hospital (Morley, 2004; Traub-Dargatz *et al.*, 2004). The major disadvantage of targeted surveillance is the inability to detect nosocomial infections in patients that are housed in other areas of the hospital, but the decreased cost and effort required for data collection counterbalances this shortcoming and surveillance efforts can be increased in patients housed in other areas of the hospital during times when an outbreak is suspected to be occurring.

Given the financial restrictions of most veterinary infection control programs and the limited personnel resources, restricting surveillance to patients believed to be at a higher risk of developing disease may be an acceptable choice. In addition to the aforementioned benefits of such an approach, the rates determined in different veterinary hospitals must be established in populations at similar risk of developing nosocomial infections in order to be compared. Also,

by limiting the scope of surveillance to a particular subset of the patient population, infection control personnel might be able to collect more information on the patients being surveyed than would be possible if collecting information on all hospitalized patients. This could lead to a more accurate assessment of the risks of infections in the surveyed population and enable determination of a valid denominator for use in data analysis.

1.4.3 Data collection and case finding methods

There are many different aspects of data collection and case finding that should be reviewed prior to designing a surveillance program. For example, data or samples used for nosocomial infection surveillance can be collected either actively or passively. Active surveillance involves the collection of data specifically for the purposes of the surveillance system, while passive surveillance involves using data collected for other purposes (Morley, 2004). The sensitivity of active data collection systems has been shown to be substantially higher than passive collection systems and this generally is considered to be the preferred method of data collection (Brachman, 1993).

Another consideration is whether data collection should occur prospectively, monitoring the patient while the patient is hospitalized, or retrospectively, reviewing the medical record after the patient is discharged (Abrutyn & Talbot, 1987). Prospective data collection is considered the gold standard by infection control programs in human medical hospitals, but there is the potential to miss occurrences of infections if they arise after the patient is

discharged (Freeman & McGowan, 1981). There have been several studies in the human medical field that have shown the importance of capturing infections that occur after discharge through surveillance, especially in identifying post-operative surgical infections (Burns & Dippe, 1982; Brown *et al.*, 1987; Fuchs, 1987; Reimer *et al.*, 1987; Law *et al.*, 1990; Delgado-Rodriguez *et al.*, 2001). However, prospective surveillance is considered to be the best method to use in order to detect potential outbreaks of nosocomial infections in real-time (Wenzel *et al.*, 1976).

Human hospitals have employed several different techniques for identifying cases of nosocomial infection prospectively. One type of system involves patient-based collection methods. This method includes case identification through direct contact with patients deemed to be at high-risk of developing infection by an infection control nurse, case identification and reporting during clinical ward rounds, and identification through the use of a “notice of infection” form that is filled out by the patient’s attending physician (Hofherr, 1979; Lynch & Jackson, 1985; Abrutyn & Talbot, 1987; Pottinger *et al.*, 1997). Another form of prospective surveillance involves diagnostic laboratory-based case identification. This method of data collection can be slower than patient-based collection methods due to the time required to culture infections and the effectiveness of this technique depends on nosocomial infections being cultured at high frequency (Abrutyn & Talbot, 1987). Additionally, laboratory-based surveillance is thought to provide less clinical data and have more false

positives and false negatives reported than patient-based surveillance (Abrutyn & Talbot, 1987).

Retrospective chart review for the purposes of identifying nosocomial infections is considered to be more time consuming and costly than is prospective data collection, but hospital readmissions for infections can be detected using this method (Pottinger *et al.*, 1997). The SENIC project did evaluate the accuracy of retrospective chart review and found the sensitivity of the technique to be similar to prospective surveillance (Haley *et al.*, 1980a). However, it has also been noted that the lack of timeliness in discovering nosocomial infections and the potential to miss clusters of infection in a single geographical area are drawbacks to this method of collection (Birnbaum & King, 1981; Glenister *et al.*, 1991).

1.4.4 Interhospital data comparison

In order to have a basis for interhospital comparison, nosocomial infection rates must be determined in several different hospitals that are collecting data in the same manner (Gaynes, 1997). However, it has previously been shown that crude rates of nosocomial infection vary with factors such as hospital size and patient characteristics, including underlying disease conditions and severity of illness (Pottinger *et al.*, 1997; Sax *et al.*, 2002). In order for valid interhospital comparisons to be made it must be determined which risk factors need to be controlled for or adjusted, possibly including length of hospitalization, exposure to devices, and intrinsic patient characteristics (Pottinger *et al.*, 1997).

1.5 Conclusions

This review shows that, unlike infection control programs in human hospitals, veterinary institutions have not yet determined the endemic or acceptable rate of nosocomial infection in hospitalized patients. Veterinary hospitals also have no defined standards for infection surveillance and control. The veterinary community must develop standard definitions for infections, standardize measurement techniques, and determine the population that should be included in infection surveillance. These items need to be addressed so that the preventable fraction of infections in veterinary institutions can be determined, and to help decide which aspects of infection control programs are effective. Some of these issues will be addressed in this thesis. The purposes of this study were to design and evaluate the use of a syndromic surveillance system for detection of nosocomial events, estimate rates of occurrence of common nosocomial events, and evaluate risk factors for the development of nosocomial events among hospitalized dog, cat, and horse patients considered to be at higher than average risk for nosocomial events in multiple veterinary referral hospitals in the United States.

2. Uniform Protocol for Surveillance

2.1 Overview

In order to collect data at multiple institutions regarding the occurrence of nosocomial infections in several species it was necessary to design a standardized surveillance system that did not interfere with established organizational structures. Each of the five participating veterinary hospitals had differently structured existing infection control programs and few of the programs had additional personnel resources to devote to data collection for this project. Therefore, it was decided that the primary clinician for each eligible case would be recruited to assist in active, prospective data collection.

2.2 Syndromic surveillance

A committee of experts in the field of veterinary infection control and biosecurity was established in order to address the logistical problems of implementing a surveillance system in multiple veterinary institutions due to the lack of available published information in the field. It was determined by this committee that clinical definitions of infection, or syndromes, would be used in order to create a low-cost surveillance system that had the benefit of rapid data collection. Although syndromic surveillance systems used for the detection of disease trends have been implemented in a limited number of situations in

veterinary medicine in the past decade, none of these systems have been developed for the detection of nosocomial infections in veterinary hospitals (Burns, 2006; Glickman *et al.*, 2006; Vourc'h *et al.*, 2006; Van Metre *et al.*, 2009). For this reason, the definitions set forth by the US CDC for the reporting of nosocomial infections in human healthcare facilities were used as a model for the definitions used in this study (Horan *et al.*, 2008). The sensitivity of this system was increased by using relevant markers of disease in the definitions of disease syndromes and by focusing on limited risk factors for development of nosocomial infection (e.g., device-associated infections). The disease syndromes included in this study were also intended to be defined and applied to all species so these data could be compared across all service areas within one hospital as well as between different facilities. Therefore, species specific syndromes, such as laminitis, were not included.

2.2.1 Nosocomial syndrome definitions

Intravenous catheter site inflammation: abnormal inflammation of the skin, subcutaneous tissues, or blood vessels at sites where indwelling catheters were placed manifested by redness, swelling, heat, drainage, or thrombosis

Abnormal urinary tract inflammation associated with urinary

catheterization: empirical evidence of urinary tract inflammation in animals that had been catheterized manifested by bacteria in urine samples, pyuria, hematuria, pollakiuria, stranguria, or urethritis

Acute infectious respiratory tract disorders: evidence of upper or lower respiratory tract disorders evidenced by coughing, sneezing, nasal discharge, abnormal lung sounds, tachypnea, or dyspnea

Acute gastrointestinal disorders: significant vomiting, diarrhea, or abdominal discomfort not predictably related to treatment

Surgery site inflammation or infection: apparent infectious problems related to surgical interventions, manifested by redness, swelling, heat, or drainage at incision site or inflammation and/or fluid accumulation at other sites

Fever of undetermined origin: temperature greater than 102.5°F in dogs and cats or greater than 102.0°F in horses that appears to be unrelated to other identifiable problems

Septicemia: clinical or microbiological evidence of bacteremia or septicemia

3. Materials and Methods

3.1 Study overview

A prospective longitudinal design was used for this study, which was conducted during a 12-week period in 2006. Dog, cat, and horse patients that were considered to be at high risk of developing nosocomial events were eligible for enrollment in the study. A surveillance form was developed to collect uniform data pertinent to each eligible patient in hard copy format. Crude rates of occurrence of nosocomial events were calculated and adjusted rates were estimated using Poisson regression. Risk factors associated with an increased risk of developing a nosocomial event were analyzed using multivariable logistic regression.

3.2 Case selection

There were a total of five participating veterinary referral hospitals (James L. Voss Veterinary Teaching Hospital at Colorado State University, The George D. Widener hospital for large animals at the University of Pennsylvania's New Bolton Center, Tufts New England Veterinary Medical Center, University of Minnesota Veterinary Medical Center, and the Veterinary Medical Teaching Hospital at the University of Missouri). Four hospitals contributed data for both small animal and horse patients and one hospital provided data only for horses.

The study was restricted to weaned (non-neonatal) patients that were hospitalized for at least one day in the respective critical care units. Additionally, in order for horse patients to be eligible for enrollment, they had to be admitted for conditions that were related to the gastrointestinal tract (either confirmed or suspected). This population of high-risk patients was selected because they were considered more likely to be exposed to potential risk factors and also more likely to have an elevated risk of occurrence of nosocomial events because of intrinsic patient risk factors.

3.3 Data collection

At the time of patient admission to the hospital the primary clinician for each eligible case was given a surveillance form to complete. The form became part of the patient record and was available for completion during the duration of hospitalization. Three types of information were collected: demographic information, procedures and treatments performed during hospitalization, and the occurrence of one or more defined nosocomial events. The form was checked for completeness after the patient was discharged and was returned to the primary clinician if it was found to be incomplete.

The demographic information collected for each patient included patient identification, species, age, gender/gender status (female, spayed female, male, or castrated male), the admitting hospital service, whether or not the patient was admitted on an emergency basis (regardless of time of admission), and the duration (in days) of hospitalization. The clinicians were asked to report if any of

the following procedures or treatments had been performed or given at any time during hospitalization: intravenous catheterization, urinary catheterization, any type of surgical procedure, devices implanted at the time of surgery, endotracheal intubation, respiratory endoscopy, gastrointestinal endoscopy, perioperative antimicrobial drugs (given within 6 hours of surgery), antimicrobial drugs administered at times other than in the perioperative period, anti-ulcer medications, and if specimens were submitted to the diagnostic laboratory to identify infectious agents. The patient's status at the end of hospitalization (either discharged alive or died/euthanized) was also recorded.

The seven previously defined nosocomial disease syndromes were also included on the survey instrument. Clinicians were asked to report if one or more of the nosocomial events occurred at one or more times after admission to the hospital. For the purpose of data analysis, each positive response regarding the occurrence of a nosocomial disease syndrome was considered a nosocomial disease event. Clinicians were instructed to report a nosocomial disease event as having occurred only if the event was unrelated to the primary reason for hospitalization and not an expected outcome from a procedure that had been performed or treatment that had been given. For example, reported events would not include diarrhea in a horse that had been admitted for suspected *Salmonella* infection or in a dog that had been admitted for suspected Parvovirus infection. Clinicians were asked to report the occurrence of nosocomial disease events without presuming whether or not the occurrence had an infectious etiology or was associated with significant morbidity in the patient.

3.4 Data analysis

The survey responses were recorded in a hard copy format and were subsequently entered into an electronic database and summarized by calculating descriptive statistics. Frequency distributions of categorical variables were evaluated. Continuous variables (age and duration of hospitalization) were analyzed by calculating means, medians, standard deviations, and ranges. Continuous variables were then categorized to facilitate analysis. Discharge status was collapsed into two categories: alive and died/euthanized. Data from each species were analyzed separately.

Crude rates of nosocomial disease events were calculated. Because baseline rates of infection have been shown to differ between hospitals, crude rates of infection were adjusted by hospital of admission (Sax and Pittet, 2002). Adjusted rates of infection (number of patients per 100 hospital days) and adjusted percentage of patients affected were estimated using Poisson regression.

Mixed effects (random slope and random intercept) logistic regression (SAS PROC GLIMMIX) was used to examine associations between potential risk factors (exposure variables) and the occurrence of nosocomial disease events (Brown and Prescott, 2006). Logistic regression was utilized due to the dichotomous outcome related to the occurrence of a nosocomial event and the mixed effects model was applied in order to account for the potential of data clustering on both the hospital and individual patient levels. The primary

outcome analyzed was the occurrence of any nosocomial disease event in a patient. Secondary outcomes that were analyzed included each of the seven individually defined nosocomial disease syndromes. Potential exposure variables that were included in the analysis were placement of intravenous or urinary catheter, respiratory endoscopy, gastrointestinal endoscopy, endotracheal intubation, surgical procedures, placement of an implant at time of surgery, antimicrobial drugs (either given perioperatively or at other times), the use of anti-ulcer medications, the patient's age and gender, the admitting hospital service, submission of samples for microbiology, if a patient was admitted to the hospital on an emergency basis, and the length of hospitalization. Patient discharge status was also evaluated. Univariable models were used to screen individual exposures. Variables that were statistically associated with the outcomes ($P \leq 0.25$) were included in multivariable model building. Final multivariable models were identified by use of a backward selection procedure with a critical α for retention of ≤ 0.05 . Two variables, placement of an intravenous catheter and any surgical procedure having been performed, were forced into the model because of their relationships with the nosocomial events intravenous catheter site inflammation and surgery site inflammation. In addition, previously excluded variables were reintroduced into the final model to insure that the exclusion was appropriate. Confounding was identified by $\geq 20\%$ change in parameter estimates when variables were individually removed from the multivariable models. When identified, confounding variables were forced into the multivariable models regardless of P -values. First order interaction terms for

main effects variables included in final models were evaluated. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated using the results of logistic regression models.

4. Results

4.1 Dogs

4.1.1 Population characteristics

Data were collected for a total of 1535 dog patients (Table 1). Mean \pm SD age of dogs was 6.5 ± 4.2 years (median, 6 years; range, 6 months to 21 years). The population was evenly distributed between males and females and the majority of the population, regardless of sex, was neutered (81%). Animals were enrolled in approximately equally numbers from the four participating hospitals (Table 1). Approximately half of the patients (56.6%) were admitted to either the medicine or surgery service of participating hospitals. The mean \pm SD length of hospitalization was 3.2 ± 3.4 days (median, 2 days; range, 1 to 48 days). Most of the patients (71.2%) were hospitalized for 3 or fewer days and 12.7% (195) were hospitalized for 6 or more days. The most commonly performed procedure was placement of an intravenous catheter. Antimicrobial drugs given at times other than perioperatively were the most commonly used medication within the study population. A large proportion of the population (41%) was admitted to the critical care unit on an emergency basis, which is consistent with this population being considered at high-risk for exposure to potential risk factors for nosocomial events. Overall, 11.1% of dog patients either died or were euthanized prior to

Table 1. Characteristics of the 1535 dog patients enrolled in the study.

Characteristics	Category	Dog (n=1535)		
		Percent (n) of all dogs	Percent (n) of dogs with any reported event (n=298)	Percent (n) of dogs with no reported nosocomial event (n=1237)
Age	Less than 1 year	9.2 (144)	8.7 (26)	9.5 (118)
	1 to 5 years	33.9 (520)	33.2 (99)	34.0 (421)
	6 to 10 years	37.6 (577)	40.3 (120)	36.9 (457)
	11 years and older	19.2 (294)	17.8 (53)	19.5 (241)
Sex	Female	9.0 (138)	9.1 (27)	9.0 (111)
	Female spayed	40.7 (625)	40.6 (121)	40.1 (504)
	Male	9.8 (151)	8.1 (24)	10.3 (127)
	Male castrated	40.3 (618)	42.3 (126)	39.8 (492)
Hospital of admission	A	23.7 (364)	20.1 (60)	24.6 (304)
	B	27.5 (422)	51.0 (152)	21.8 (270)
	C	27.9 (428)	20.1 (60)	29.8 (368)
	D	20.9 (321)	8.7 (26)	23.9 (295)
Length of hospitalization	1 day	26.8 (411)	15.8 (47)	29.4 (364)
	2 days	28.1 (432)	21.1 (63)	29.8 (369)
	3 days	16.3 (250)	15.8 (47)	16.4 (203)
	4 days	9.1 (139)	10.4 (31)	8.7 (108)
	5 days	7.0 (108)	9.4 (28)	6.5 (80)
	6 or more days	12.7 (195)	27.5 (82)	9.1 (113)
Procedures and medications of interest	Intravenous catheter	98.2 (1508)	99.7 (297)	97.9 (1211)
	Urinary Catheter	18.2 (280)	32.2 (96)	14.9 (184)
	Surgical procedure	42.2 (647)	53.4 (159)	39.5 (488)
	Implant placed during surgery	11.3 (174)	9.4 (28)	11.8 (146)
	Endotracheal intubation	47.7 (732)	54.4 (162)	46.1 (570)
	Respiratory Endoscopy	1.8 (28)	2.0 (6)	1.8 (22)
	Gastrointestinal Endoscopy	1.8 (28)	2.0 (6)	1.8 (22)
	Peri-operative antimicrobials	33.4 (512)	32.2 (96)	33.6 (416)
	Antimicrobials (not peri-operative)	48.9 (750)	65.1 (194)	45.0 (556)
	Anti-ulcer medications	33.6 (515)	53.0 (158)	28.9 (357)
	Samples submitted for microbiology	22.5 (346)	38.6 (115)	18.7 (231)
Agents recovered from sample submission	11.0 (169)	24.5 (73)	7.8 (96)	
Patient admitted on an emergency basis	Yes	41.0 (630)	37.3 (111)	42.0 (519)
	No	59.0 (905)	62.8 (187)	58.0 (718)
Discharge Status	Alive	88.9 (1365)	89.6 (267)	88.8 (1098)
	Died/Euthanized	11.1 (170)	10.4 (31)	11.2 (139)

discharge, which provides an indication of the severity of illness in the study population.

4.1.2 Occurrence of nosocomial events – Crude Rates

Four hundred thirty-nine nosocomial events were reported to have occurred in 19.4% (298/1535) dog patients. Individual hospitals had wide variability in the reported occurrence of any nosocomial event in patients admitted to the study, which ranged from 8.1% (26/321) to 36.0% (152/422). The most often reported individual nosocomial event was surgical site inflammation, which occurred in 14.4% (93/647) of the dog patients that underwent a surgical procedure. Surgical site inflammation was reported to have occurred in as few as 3.9% (4/102) of dog patients and as many as 37.8% (51/135) of the patients at individual institutions. Urinary tract inflammation was reported to have occurred in 11.4% (32/280) of the patients that had a urinary catheter placed. Rates of occurrence of urinary tract inflammation associated with urinary catheterization at individual institutions varied from 4.6% (4/87) to 17.3% (19/110). Of the dogs that had an intravenous catheter placed 6.7% (101/1508) were reported to have inflammation at the site of catheterization, with rates from individual institutions ranging from 4.1% (14/418) to 12.8% (53/415) of patients. Significant gastrointestinal disorders were reported in 5.4% (83/1535) of the dogs in this study, with a range from 1.2% (4/321) to 10.2% (43/422) of the patients admitted at individual institutions. Fever of undetermined origin was reported in 4.8% (74/1535) of patients, varying from 0.9% (4/428) to 12.6% (53/422) of patients from an individual institution. Acute respiratory disorders were reported in 2.2% (34/1535) of patients, rates from individual institutions ranged from 0.5% (2/428) to 5.2% (22/422). Septicemia was reported to have occurred in 1.6%

(24/1535) of patients, the range from individual institutions was 1.4% (5/364) to 1.9% (8/428).

4.1.3 Occurrence of nosocomial events – Hospital adjusted rates

Overall, hospital adjusted rates of occurrence of nosocomial events were slightly lower than the crude rates of occurrence (Table 2). Nosocomial events were detected in 5.2 patients (95% CI, 4.6 to 6.0) per 100 days of hospitalization. While prevalence rates for specific events differed widely, the incidence rates per 100 days of hospitalization were much less variable (Table 2).

Table 2. Nosocomial events occurring in dog patients after hospital admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.

Syndrome (Case definition)	Percent (95% CI) of affected patients ¹	Incidence (95% CI) of events ²
Any Event	16.3 (14.3, 18.5)	5.2 (4.6, 6.0)
IV catheter site inflammation (abnormal inflammation of the skin, subcutaneous tissues, or blood vessels at sites where indwelling catheters were placed manifested by redness, swelling, heat, drainage, or thrombosis)	5.5 (4.4, 6.9)	1.8 (1.4, 2.2)
Urinary Tract Inflammation (empirical evidence of urinary tract inflammation in animals that had been catheterized manifested by bacteria in urine samples, pyuria, hematuria, pollakiuria, stranguria, or urethritis)	7.4 (4.5, 12.2)	1.8 (1.1, 2.9)
Acute Respiratory disorders (evidence of upper or lower respiratory tract disorders evidenced by coughing, sneezing, nasal discharge, abnormal lung sounds, tachypnea, or dyspnea)	1.6 (1.1, 2.5)	0.5 (0.4, 0.8)
GI disorders (significant diarrhea, vomiting, or abdominal discomfort not predictably related to treatment)	4.0 (3.0, 5.3)	1.3 (1.0, 1.7)
Surgical site inflammation (apparent infectious problems related to surgical interventions, manifested by redness, swelling, heat, or drainage at incision site or inflammation and/or fluid accumulation at other sites)	10.1 (7.4, 13.7)	2.8 (2.1, 3.9)
Fever of unknown origin (temperature greater than 102.5°F that appears to be unrelated to other identifiable problems)	3.1 (2.3, 4.3)	1.0 (0.7, 1.4)
Septicemia (clinical or microbiological evidence of bacteremia or septicemia)	1.6 (1.0, 2.3)	0.5 (0.3, 0.7)

¹-Proportion of patients with events among those affected adjusted for hospital of admission

²-Number of patients affected per 100 days of hospitalization adjusted for hospital of admission

4.1.4 Risk factors for nosocomial events

In general, the final multivariable models for each of the individually defined nosocomial syndromes were very similar to the final multivariable model investigating factors associated with the occurrence of any nosocomial event. Therefore, only results for the multivariable model with the primary outcome being the occurrence of any nosocomial event are presented here. Exposure variables meeting entry criteria for multivariable model selection of factors related to the outcome of any nosocomial event were intravenous catheterization, urinary catheterization, surgical procedures, endotracheal intubation, gastrointestinal endoscopy, peri-operative antimicrobial drugs, antimicrobial drugs given at times other than peri-operatively, anti-ulcer medications, and duration of hospitalization. Variables retained in the model after the backward selection procedure were intravenous catheterization, urinary catheterization, surgical procedure, antimicrobial drugs given at times other than peri-operatively, anti-ulcer medications, and duration of hospitalization (Table 3). The exposure variable intravenous catheterization did not reach the critical α for retention, but was retained in the model due to the relation between the variable and the outcome of inflammation associated with intravenous catheterization. Interaction terms for main effects were not significant when included in the final model.

Risk factors of specific procedures that were associated with increased risk of any nosocomial event being reported were surgical procedures and placement of a urinary catheter (Table 3). Treatment with anti-ulcer medications and antimicrobial drugs given at times other than peri-operatively were also

Table 3. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of any nosocomial event in dog patients.

Variable	Category	Odds Ratio	95% CI	P-value
Any surgical procedure	Yes	2.18	1.62, 2.93	<.0001
	No		Reference	
Anti-ulcer medications	Yes	2.60	1.92, 3.52	<.0001
	No		Reference	
Urinary Catheter	Yes	1.60	1.15, 2.22	0.0053
	No		Reference	
Antimicrobials (not peri-operative)	Yes	1.81	1.33, 2.46	0.0002
	No		Reference	
Length of hospitalization	6 or more days	3.02	2.08, 4.39	<.0001
	4 to 5 days	1.23	0.85, 1.79	
	1 to 3 days		Reference	
IV Catheter	Yes	3.71	0.48, 28.86	0.2102
	No		Reference	

associated with increased risk of developing a nosocomial event. Increased duration of hospitalization, though a non-specific indicator of risk, was positively associated with increased odds that a nosocomial event would be reported (Table 3).

4.2 Cats

4.2.1 Population characteristics

Data were collected for a total of 416 cat patients (Table 4). Mean \pm SD age of cats was 7.9 ± 4.9 years (median, 7 years; range, 6 months to 23 years).

Table 4: Characteristics of the 416 cat patients enrolled in the study

Characteristics	Category	Cat (n=416)		
		Percent (n) of all cats	Percent (n) of cats with any reported event (n=67)	Percent (n) of cats with no reported nosocomial event (n=349)
Age	Less than 1 year	5.5 (23)	4.5 (3)	5.7 (20)
	1 to 5 years	30.5 (127)	37.3 (25)	29.2 (102)
	6 to 10 years	32.0 (133)	32.8 (22)	31.8 (111)
	11 years and older	32.0 (133)	25.4 (17)	33.2 (116)
Sex	Female	7.0 (29)	6.0 (4)	7.2 (25)
	Female spayed	35.3 (147)	23.9 (16)	37.5 (131)
	Male	2.4 (10)	4.5 (3)	2.0 (7)
	Male castrated	55.1 (229)	65.7 (44)	53.0 (185)
Hospital of admission	A	15.1 (63)	11.9 (8)	15.8 (55)
	B	40.1 (167)	68.7 (46)	34.7 (121)
	C	17.8 (74)	4.5 (3)	20.3 (71)
	D	26.9 (112)	14.9 (10)	29.2 (102)
Length of hospitalization	1 day	26.2 (109)	16.4 (11)	28.1 (98)
	2 days	26.2 (109)	20.9 (14)	27.2 (95)
	3 days	17.1 (71)	9.0 (6)	18.6 (65)
	4 days	9.9 (41)	11.9 (8)	9.5 (33)
	5 days	8.4 (35)	17.9 (12)	6.6 (23)
	6 or more days	12.3 (51)	23.9 (16)	10.0 (35)
Procedures and medications of interest	Intravenous catheter	97.4 (405)	100 (67)	96.9 (338)
	Urinary Catheter	17.1 (71)	40.3 (27)	12.6 (44)
	Surgical procedure	21.4 (89)	46.3 (31)	16.6 (58)
	Implant placed during surgery	5.5 (23)	11.9 (8)	4.3 (15)
	Endotracheal intubation	27.9 (116)	50.8 (34)	23.5 (82)
	Respiratory Endoscopy	1.7 (7)	4.5 (3)	1.2 (4)
	Gastrointestinal Endoscopy	1.7 (7)	3.0 (2)	1.4 (5)
	Peri-operative antimicrobials	14.7 (61)	19.4 (13)	13.8 (48)
	Antimicrobials (not peri-operative)	53.1 (221)	68.7 (46)	50.1 (175)
	Anti-ulcer medications	33.7 (140)	62.7 (42)	28.1 (98)
	Samples submitted for microbiology	28.6 (119)	41.8 (28)	26.1 (91)
Agents recovered from sample submission	15.4 (64)	31.3 (21)	12.3 (43)	
Patient admitted on an emergency basis	Yes	52.9 (220)	50.8 (34)	53.3 (186)
	No	47.1 (196)	49.3 (33)	46.7 (163)
Discharge Status	Alive	85.1 (354)	74.6 (50)	87.1 (304)
	Died/Euthanized	14.9 (62)	25.4 (17)	12.9 (45)

The population was approximately evenly distributed between males and females and the majority of the population, regardless of sex, was neutered (90.4%).

Forty percent (167/416) of the subjects enrolled in the study were from one of the

participating hospitals, the other hospitals contributed from 15.1% (63/416) to 26.9% (112/416) of the enrolled subjects. The mean length of hospitalization for cats was 3.3 ± 3.4 days (median, 2 days; range, 1 to 36 days). Most of the patients (69.5%) were hospitalized for 3 or fewer days and 12.3% (51) were hospitalized for 6 or more days. The most commonly performed procedure was placement of an intravenous catheter. Antimicrobial drugs given at times other than peri-operatively were the most commonly used medication within the study population. A large proportion of the population (52.9%) was admitted to the critical care unit on an emergency basis which is consistent with this population being considered high-risk for exposure to potential risk factors for nosocomial events. The severity of illness in the study population is indicated by the overall mortality rate of 14.9%.

4.2.2 Occurrence of nosocomial events – Crude Rates

Ninety-eight nosocomial events were reported to have occurred in 16.1% (67/416) of cat patients. Individual hospitals had wide variability in the reported occurrence of any nosocomial event in patients admitted to the study, which ranged from 4.1% (3/74) to 27.5% (46/167). The most often reported individual nosocomial event was urinary tract inflammation associated with placement of a urinary catheter. Urinary tract inflammation was reported to have occurred in 15.5% (11/71) of the cats that had a urinary catheter placed, but all of the cases were reported from only two institutions, with rates of 5.9% (1/17) and 31.7% (13/41) respectively. Surgical site inflammation was reported to have occurred in 10.1% (9/89) of the cat patients that underwent a surgical procedure,

but all reports of inflammation at the surgical site came from one institution where 27.3% (9/33) of their surgical patients were affected. Of the cats that had an intravenous catheter placed, 5.7% (23/405) were reported to have inflammation at the site of catheterization, with rates from individual institutions ranging from 0.9% (1/110) to 11.7% (19/162) of patients. Significant gastrointestinal disorders were reported in 4.1% (17/416) of the cats in this study, rates from individual institutions ranging from having no cases reported to 8.4% (14/167) of the patients affected. Fever of undetermined origin was reported in 5.3% (22/416) of patients, varying from 1.4% (1/74) to 9.0% (15/167) of patients from an individual institution. Acute respiratory disorders were reported in 3.4% (14/416) of patients, rates from individual institutions ranged from 1.4% (1/74) to 4.8% (8/167). Septicemia was reported to have occurred in 0.01% (2/416) of patients and all cases were reported from only 2 institutions.

4.2.3 Occurrence of nosocomial events – Hospital adjusted rates

Overall, hospital adjusted rates of occurrence of nosocomial events were slightly lower than the crude rates of occurrence (Table 5). Nosocomial events were detected in 3.7 patients (95% CI, 2.9 to 4.8) per 100 days of hospitalization. While prevalences for specific events differed widely (from 0.5% to 9.0%), the incidence rates per 100 days of hospitalization were much less variable (Table 5).

4.2.4 Risk factors for nosocomial events

In general, the final multivariable models for each of the individually

Table 5. Nosocomial events occurring in cat patients after hospital admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.

Syndrome (Case definition)	Percent (95% CI) of affected patients ¹	Incidence (95% CI) of events ²
Any Event	12.0 (9.3, 15.5)	3.7 (2.9, 4.8)
IV catheter site inflammation (abnormal inflammation of the skin, subcutaneous tissues, or blood vessels at sites where indwelling catheters were placed manifested by redness, swelling, heat, drainage, or thrombosis)	4.0 (2.6, 6.2)	1.2 (0.8, 1.9)
Urinary Tract Inflammation (empirical evidence of urinary tract inflammation in animals that had been catheterized manifested by bacteria in urine samples, pyuria, hematuria, pollakiuria, stranguria, or urethritis)	9.0 (4.3, 18.5)	2.4 (1.2, 5.0)
Acute Respiratory disorders (evidence of upper or lower respiratory tract disorders evidenced by coughing, sneezing, nasal discharge, abnormal lung sounds, tachypnea, or dyspnea)	2.1 (1.1, 3.8)	0.6 (0.3, 1.2)
GI disorders (significant diarrhea, vomiting, or abdominal discomfort not predictably related to treatment)	2.7 (1.6, 4.5)	0.8 (0.5, 1.4)
Surgical site inflammation (apparent infectious problems related to surgical interventions, manifested by redness, swelling, heat, or drainage at incision site or inflammation and/or fluid accumulation at other sites)	5.4 (2.7, 10.9)	1.5 (0.7, 3.0)
Fever of unknown origin (temperature greater than 102.5°F that appears to be unrelated to other identifiable problems)	2.7 (1.6, 4.4)	0.8 (0.5, 1.3)
Septicemia (clinical or microbiological evidence of bacteremia or septicemia)	0.5 (0.1, 2.0)	0.2 (0.04, 0.6)

1-Proportion of patients with events among those affected adjusted for hospital of admission

2-Number of patients affected per 100 days of hospitalization adjusted for hospital of admission

defined nosocomial syndromes were very similar to the final multivariable model investigating factors associated with the occurrence of any nosocomial event. Therefore, only results for the multivariable model with the primary outcome being the occurrence of any nosocomial event are presented here. Exposure variables meeting entry criteria for multivariable model selection of factors related to the outcome of any nosocomial event were sex/sex status, urinary catheterization, surgical procedures, device implanted at time of surgery, endotracheal intubation, respiratory endoscopy, gastrointestinal endoscopy, antimicrobial drugs given peri-operatively, antimicrobial drugs given at times other than peri-operatively, anti-ulcer medications, and duration of hospitalization. Variables retained in the model after the backward selection

procedure were intravenous catheterization, urinary catheterization, surgical procedure, and anti-ulcer medications (Table 6). The exposure variable intravenous catheterization did not reach the critical α for retention, but was retained in the model due to the relation between the variable and the outcome of inflammation associated with intravenous catheterization. Interaction terms for main effects were not significant when included in the final model.

Table 6. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of any nosocomial event in cat patients.

Variable	Category	Odds Ratio	95% CI	P -value
Any surgical procedure	Yes	4.53	2.34, 8.74	<0.0001
	No		Reference	
Anti-ulcer medications	Yes	3.89	2.06, 7.32	<0.0001
	No		Reference	
Urinary Catheter	Yes	2.96	1.49, 5.88	0.0020
	No		Reference	
IV Catheter	Yes	0.55	0.06, 4.74	0.5810
	No		Reference	

The risk factor for a specific procedure that was associated with the greatest increase in the risk for any nosocomial event being reported was undergoing any type of surgical procedure (Table 6). Nosocomial events were reported for each of the seven defined nosocomial events in cats that had surgery, with the most commonly reported events being inflammation at the surgical site, fever of undetermined origin, and urinary tract inflammation. Placement of a urinary catheter was also associated with increased risk of any nosocomial event being reported. Specific nosocomial events reported in cats

that had a urinary catheter placed included each of the seven defined events. Treatment with anti-ulcer medications was associated with increased risk of any nosocomial event being reported (Table 6). Non-specific indicators of health, such as age or duration of hospitalization, were not associated with increased risk of occurrence of nosocomial events.

4.3 Horses

4.3.1 Population characteristics

Data were collected for a total of 297 horses (Table 7). Mean \pm SD age of the study population was 9.1 ± 6.5 years (median 8 years; range, 6 months to 31 years). Nearly a third of the subjects enrolled in the study were from one of the participating hospitals, the other hospitals contributed from 7.7 to 27.3 percent of the enrolled subjects. The majority of patients (86.2%) were admitted to either the medicine or surgery service of participating hospitals before subsequently being admitted to the critical care unit. Approximately half (53.9%) of the population was admitted to the critical care unit on an emergency basis. Half of the patients (50.2%) were hospitalized for 3 or fewer days and 25.3% (75) of the study population was hospitalized for 7 or more days. The most commonly performed procedure was placement of an intravenous catheter. Antimicrobial drugs given at times other than perioperatively were the most commonly used medication within the study population. The mortality rate of all horses in the study population was 9.4%. Within individual institutions, mortality rates ranged from 4.3% to 13.0%.

Table 7. Characteristics of the 297 horse patients enrolled in the study.

Characteristics	Category	Percent (n) of all patients	Percent (n) of patients with any reported nosocomial event (n=65)	Percent (n) of patients with no reported nosocomial event (n=232)
Age ¹	Less than 1 year	7.7 (23)	10.8 (7)	6.9 (16)
	1 to 5 years	26.9 (80)	30.8 (20)	25.9 (60)
	6 to 10 years	30.6 (91)	23.1 (15)	32.8 (76)
	11 years and older	34.7 (103)	35.4 (23)	34.5 (80)
Sex	F	35.0 (104)	35.4 (23)	34.9 (81)
	FS	0.7 (2)	-	0.9 (2)
	M	19.2 (57)	33.9 (22)	15.1 (35)
	MC	45.1 (134)	30.8 (20)	49.1 (114)
Hospital	A	10.4 (31)	13.9 (9)	9.5 (22)
	B	23.2 (69)	21.5 (14)	23.7 (55)
	C	27.3 (81)	10.8 (7)	31.9 (74)
	D	7.7 (23)	6.2 (4)	8.2 (19)
	E	31.3 (93)	47.7 (31)	26.7 (62)
Patients admitted on an emergency basis	Yes	53.9 (160)	61.5 (40)	51.7 (120)
	No	46.1 (137)	38.5 (25)	48.3 (112)
Length of hospitalization	1 to 3 days	50.2 (149)	12.3 (8)	60.8 (141)
	4 to 6 days	24.6 (73)	21.5 (14)	25.4 (59)
	7 or more days	25.3 (75)	66.2 (43)	13.8 (32)
Procedures and medications of interest ²	IV catheter	92.3 (274)	98.5 (64)	90.5 (210)
	Urinary Catheter	7.4 (22)	21.5 (14)	3.5 (8)
	Surgery	28.6 (85)	52.3 (34)	22.0 (51)
	Implant placed	1.7 (5)	3.1 (2)	1.3 (3)
	Intubation	26.9 (80)	52.3 (34)	19.8 (46)
	Respiratory Endoscopy	2.7 (8)	6.2 (4)	1.7 (4)
	GI Endoscopy	14.1 (42)	12.3 (8)	14.7 (34)
	Peri-operative antimicrobials	28.6 (85)	52.3 (34)	22.0 (51)
	Antimicrobials (non-peri-operative)	42.8 (127)	80.0 (52)	32.3 (75)
	GI protectants	26.9 (80)	36.9 (24)	24.1 (56)
	Samples sent to DLab	58.9 (175)	87.7 (57)	50.9 (118)
	Agents recovered from Dlab submission	12.8 (38)	32.3 (21)	7.3 (17)
Discharge Status	Alive	90.6 (269)	87.7 (57)	91.4 (212)
	Died/Euthanized	9.4 (28)	12.3 (8)	8.6 (20)

1 - 3 values missing

2- Not mutually exclusive categories

4.3.2 Occurrence of nosocomial events – Crude Rates

Ninety-five nosocomial events were reported to have occurred in 21.9% (65/297) of the study population. Individual hospitals had wide variability in the reported occurrence of any nosocomial event in patients admitted to the study, which ranged from 8.6% (7/81) to 33.3% (31/93). The most often reported individual nosocomial event was surgical site inflammation, which occurred in

12.9% (11/85) of the patients that underwent a surgical procedure. Surgical site inflammation was reported to have occurred in as few as 5% (1/20) and as many as 30% (3/10) of the patients at individual institutions. Significant gastrointestinal disorders were reported in 9.1% (27/297) of the horses in this study, with a range from 2.5% (2/81) to 16.1% (5/31) of the patients admitted at individual institutions. Of the horses that had an intravenous catheter placed 8.8% (24/274) were reported to have inflammation at the site of catheterization, with rates from individual institutions ranging from 5.1% (4/78) to 33.3% (31/93) of patients. Fever of undetermined origin was reported in 5.1% (15/297) of patients, varying from no cases reported to 10.8% (10/93) of patients from an individual institution. Septicemia was reported to have occurred in 4.7% (14/297) of patients and all cases were reported from only two institutions. Acute respiratory disorders were reported in 1.4% (4/297) of patients, all cases were reported to have occurred at two institutions. Urinary tract inflammation was not reported to have occurred in any horse patients in this study.

4.3.3 Occurrence of nosocomial events – Hospital adjusted rates

Overall, hospital adjusted rates of occurrence of nosocomial events were slightly lower than the crude rates of occurrence (Table 8). It was not possible to estimate the adjusted rates of occurrence of fever of undetermined origin, acute respiratory disorders, or septicemia due to the rarity of cases with these diagnoses in the population. Overall, nosocomial events were detected in 3.9 patients per 100 days of hospitalization (95% CI, 2.9 to 4.3). While hospital

adjusted rates of occurrence for specific events differed, the incidences per 100 days of hospitalization were approximately equal (Table 8).

Table 8. Nosocomial events occurring in horses after admission and not related to the primary reason for hospitalization or an expected outcome of treatment as reported by the primary clinician.

Syndrome (Case definition)	Percent of affected patients ¹	Incidence of events ²
Any Event	19.7 (14.5, 26.7)	3.9 (2.9, 4.3)
Surgical site inflammation (apparent infectious problems related to surgical interventions, manifested by redness, swelling, heat, or drainage at incision site or inflammation and/or fluid accumulation at other sites)	12.4 (6.3, 24.4)	1.6 (0.8, 3.1)
IV catheter site inflammation (abnormal inflammation of the skin, subcutaneous tissues, or blood vessels at sites where indwelling catheters were placed manifested by redness, swelling, heat, drainage, or thrombosis)	8.6 (5.4, 13.7)	1.7 (1.0, 2.6)
GI disorders (significant diarrhea or abdominal discomfort not predictably related to treatment)	7.4 (4.3, 12.8)	1.5 (0.9, 2.5)
Fever of unknown origin (temperature greater than 102.5°F that appears to be unrelated to other identifiable problems)	<0.1	0
Acute Respiratory disorders (evidence of upper or lower respiratory tract disorders evidenced by coughing, sneezing, nasal discharge, abnormal lung sounds, tachypnea, or dyspnea)	0	0
Septicemia (clinical or microbiological evidence of bacteremia or septicemia)	0	0
Urinary Tract Inflammation (empirical evidence of urinary tract inflammation in animals that had been catheterized manifested by bacteria in urine samples, pyuria, hematuria, pollakiuria, stranguria, or urethritis)	0	0

1-Proportion of patients with events among those affected adjusted for hospital of admission

2-Number of patients affected per 100 days of hospitalization adjusted for hospital of admission

4.3.4 Risk factors for nosocomial events

In general, the final multivariable models for each of the individually defined nosocomial syndromes were very similar to the final multivariable model investigating factors associated with the occurrence of any nosocomial event. Therefore, only results for the multivariable model with the primary outcome being the occurrence of any nosocomial event are presented here. Exposure variables meeting entry criteria for multivariable model selection of factors related

to the outcome of any nosocomial event were intravenous catheterization, urinary catheterization, any surgical procedure, endotracheal intubation, respiratory endoscopy, perioperative antimicrobial drugs, antimicrobial drugs given non-perioperatively, gastrointestinal protectant medications, length of hospitalization, and sex/status of the patient. After the backward selection procedure was completed, variables retained in the model were urinary catheterization, length of hospitalization, and sex of the patient (Table 9). The exposure variables intravenous catheterization and any surgical procedure having been performed did not reach the critical α for retention, but were retained in the model due to the relation between the variables and the outcomes of inflammation associated with intravenous catheterization or at the location of a surgical site.

The only risk factor of a specific procedure that was associated with an increased risk of any nosocomial event being reported in a patient was placement of a urinary catheter. However, none of the patients that had a urinary catheter placed developed a urinary tract infection, which would be a potential nosocomial event that could be caused by introduction of bacteria to the urinary tract during this procedure. In this study population, this procedure is likely reflective of the degree of severity of disease in those patients rather than a causative mechanism in the development of a nosocomial event. Other factors associated with the development of a nosocomial syndrome were non-specific indicators of risk, such as length of hospital stay and gender.

Table 9. Results for the final multivariable logistic regression model for risk factors associated with the occurrence of a nosocomial event in horse patients.

Variable	Category	Odds Ratio	95% CI	<i>P</i> -value
Length of hospitalization	7 or more days	18.35	6.88, 48.94	<.0001
	4 to 6 days	3.57	1.33, 9.57	
	1 to 3 days		Reference	
Urinary Catheter	Yes	4.77	1.11, 20.59	0.0366
	No		Reference	
Sex	F	2.09	0.84, 5.18	0.0122
	M	4.19	1.64, 10.73	
	MC		Reference	
IV Catheter	Yes	6.33	0.63, 63.60	0.1164
	No		Reference	
Surgery	Yes	0.987	0.43, 2.24	0.9747
	No		Reference	

5. Discussion and Conclusions

The syndromic surveillance system used in this study was implemented in multiple veterinary institutions with little to no interference with each institution's established organizational structure. Active data collection was performed prospectively by attending clinicians and no additional personnel were required to perform the surveillance. The data collection system was considered easy to use and, as it was implemented in this study, added very little cost to the operating budget of participating hospitals.

There are, however, limitations to the system used in this study. One such limitation is that the surveillance forms were provided to clinicians in a paper format, and that did slow the process for data collection due to the need to enter data manually into a database. Future work could benefit from the use of an electronic reporting system that would allow data to be accessed more rapidly. Another limitation is that the definitions used for the nosocomial events reported in this study were based upon human definitions of nosocomial events. Further work in this area should be completed in order to determine if these definitions are clinically relevant to veterinary patients. It should also be determined if species-specific events, such as laminitis, are appropriate to include in definitions for syndromic surveillance.

Using this syndromic surveillance system, the rates of occurrence of any nosocomial event as well as the rates of occurrence of seven specific disease syndromes were able to be estimated in dogs, cats, and horses in several veterinary referral hospitals simultaneously. It is not possible to know, however, if the overall percentage of patients affected by nosocomial events or the incidence rates determined in this study should be considered high rates of occurrence or low rates of occurrence due to the scarcity of previously reported data. However, the rates determined in this study do suggest that nosocomial infection rates may be more of a problem in veterinary medicine than has been previously reported.

This study does show that the rate of occurrence of any nosocomial event is higher in horses than in dogs and higher in dogs than in cats. It is unknown whether these differences are due to disparities in infection control practices when handling different species or if horses and dogs are more susceptible to developing a nosocomial event during hospitalization than are cats. There was also a great deal of variability in rates determined at different institutions. This may suggest that infection control practices are more effective at some institutions than others and a portion of the events detected in this study could have been preventable if more effective infection control practices had been implemented. Another possibility is that the caseload of some hospitals included patients with higher intrinsic risk of developing nosocomial infections than other hospitals participating in this study. Inclusion of analysis of patient intrinsic risk

factors in future work would help to determine the reasons for the variability in rates between individual hospitals.

In the study reported here we found positive associations between increased hospital stay, surgical procedures having been performed, and placement of a urinary catheter with the development of a nosocomial event, which is consistent with previous studies in both veterinary and human literature (Richards *et al.*, 2000; Smyth and Emmerson, 2000; Eugster *et al.*, 2004; Smarick *et al.*, 2004; Ogeer-Gyles *et al.*, 2006). Positive associations were also identified between the administration of antimicrobial drugs at times other than peri-operatively and the use of anti-ulcer medications and the development of a nosocomial event. However, because data were collected at the time of patient discharge it is not possible to determine if medications were given before or after the nosocomial event occurred. Previous studies have shown that the use of antimicrobials and anti-ulcer medications are associated with nosocomial events presumably due to the disruption of the intestinal microflora (Bignardi, 1998; Barbut and Petit, 2001; Coté and Howden, 2008; Clooten *et al.*, 2008; Owens *et al.*, 2008). More specific risk factors were found for dogs than for cats or horses, but the risk factors identified for cat and horse patients were associated with higher odds of acquiring a nosocomial event than were the risk factors determined in dogs.

The results of this study suggest that syndromic surveillance systems can be effectively implemented in multiple veterinary institutions for the determining the rates of occurrence of nosocomial infection. The use of this type of system

as an ongoing part of hospital operations could be a valuable tool in early detection of nosocomial outbreaks in veterinary hospitals. Furthermore, implementation of an ongoing standardized surveillance system in multiple institutions will allow for comparison of rates between institutions, which would be beneficial in determining which infection control practices are most useful for the prevention of nosocomial infections in veterinary patients.

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