THE EFFECT OF THREE TYPES OF ENDOTRACHEAL TUBES ON VENTILATOR-ASSOCIATED PNEUMONIA

by

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submitted in accordance with the requirements

for the degree

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STUDY LEADER: Prof Y Botma

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DECLARATION BY THE CANDIDATE

I, Maria Jacoba Johanna Phillips, declare that the dissertation on THE EFFECT OF THREE TYPES OF ENDOTRACHEAL TUBES ON VENTILATOR ASSOCIATED PNEUMONIA hereby submitted by me for the masters degree at the University of the Free State is my own independent work and has not previously been submitted by me at another university/faculty. I furthermore cede copyright of the dissertation in favour of the University of the Free State.

_____ 30 November 2004

SIGNATURE Date

(Mrs Maria Jacoba Johanna Phillips)
Student number: 1982035477

To my husband

Patrick

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SUMMERY

Ventilator-associated pneumonia is associated with a high mortality, morbidity and medical cost and is common and has major complications. Prevention of ventilator-associated pneumonia is dependent on how well we understand the pathogeneses of the disease. The pathogeneses starts with the colonization of the upper airway and the gastrointestinal tract, pooling of secretions in the subglottic space and aspiration of this contaminated secretions past the endotracheal cuff (endogenous source of pathogens). As the host's defences are overcome, tventilator-associated pneumonia develops. Newer types of endotracheal tubes were designed with a dorsal lumen for the removal of subglottic secretions. This prevents the aspiration of contaminated secretion into the lower sterile airways. The aim of this research was to determine the effect of three types of endotracheal tubes on ventilator-associated pneumonia.

A single center, blind, prospective, controlled clinical trial has been selected to investigate the effect of three types of endotracheal tubes on ventilator-associated pneumonia.

Prior to the commencement of the study, approval for the performance of the study was obtained from the Ethics Committee of the Faculty of Health Sciences of the University of the Free State, the Universitas hospital, the manager of the intensive care units and neurosurgical intensive care unit as well as from the head of the neurosurgical department.

Informed consent was obtained from candidates or if the candidates were unable to provide consent from their spouse, child or parent and information regarding the purpose, procedure, and possible adverse effects relevant to the study, were provided. Written consent was obtained. If the candidates was unable to give consent themselves and their family was unavailable, the researcher obtained telephonic consent from above-mentioned family members. The consent forms were available in Afrikaans, English and South-Sotho. If the subject did not understand English or Afrikaans, the researcher made use of a registered nurse as a translator to explain the purpose, procedure, and possible adverse effects relevant to the study. A witness co-signed all consent forms.

Seventy-one candidates that met the inclusion criteria were screened for enrolment into the study. Thirty-four of these candidates were successfully enrolled. Subjects were consecutively allocated into three study groups. Each study group was intubated with the type of endotracheal tube for the specific study group and studied for the development of ventilator-associated pneumonia. The two experimental groups were subjected to two hourly subglottic suctioning. One experimental group's cuff pressures were measured and maintained within normal limits, whereas a Lanz™ valve maintained the other experimental group's cuff pressures. The control group was intubated with the conventional type of endotracheal tube. The implementation took place over a period of 18-months.

Data was statistically analysed and presented by means of frequencies, medians and comparison of 95% confidence intervals. This study has found that none of the subjects in the experimental groups (received subglottic suctioning) developed late-onset ventilator-associated pneumonia compared to 16.67% in the control group. The incidence of early-onset ventilator-associated pneumonia was also much higher (75%) in the control group than the experimental groups. The relative risk for late-onset ventilator-associated pneumonia indicated that subglottic suctioning was not a preventative factor in the prevention of late-onset ventilator-associated pneumonia in the experimental groups.

The time of intubation of the control group was longer than the two experimental groups. No significant difference was found in the morbidity and the mortality of the three study groups.

Recommendations are that the study should be repeated with a larger study group and the subjects should be ventilated for a longer period. The benefits of subglottic suctioning may present it more clearly. The benefits of the Lanz™ valve have not been investigated sufficiently in this study.

In closing a repetition of some wise words:

"Keep an open mind toward pneumonia. Our grandchildren will be interested and are likely to have as many differences of opinion…as we have."
William Osler. 1900 (Craven & Steger, 1995:1S)

OPSOMMING

Ventilator-geassosieerde pneumonie word geassosieer met ‘n hoë sterftesyfer, morbiditeit asook hoë mediese koste en is bekend vir erge komplikasies. ‘n Insig in die patogenese van die siekte is noodsaaklik om ventilator-geassosieerde pneumonie te voorkom. Die patogenese begin met kolonisasie van die boonste lugweg en die gastroïntestinale kanaal, opeenhoping van sekresies in die subglotiese ruimte sowel as aspirasie van hierdie gekontamineerde sekresies verby die endotrageale mansjet (endogene bron van patogene). Ventilator-geassosieerde pneumonie ontwikkel namate die gasheer se verdedigingsmeganismes afgebreek word. Nuwe soorte endotrageale buise wat aspirasie van gekontamineerde sekresie in die onderste steriele lugweë voorkom deur middel van ‘n dorsale opening waardeur subglotale sekresie verwyder kan word, is ontwerp.

‘n Enkel sentrum, blinde, prospektiewe, kontrole kliniese proef is vir die doel van die studie gekies om ondersoek in te stel na die effek van drie soorte endotrageale buise in ventilator-geassosieerde pneumonie.

Voor die aanvang van die studie, is goedkeuring vir die uitvoering van die studie van die Etiek Komitee van die Fakulteit Gesondheidswetenskappe van die Universiteit van die Vrystaat verkry. Verdere goedkeuring is verkry van Universitas hospitaal, die bestuurder van die intensiewe sorg eenhede en die neurochirurgiese intensiewesorg eenheid sowel as van die hoof van die departement neurochirurgie.

Geskrewe ingeligte toestemming aangaande die doel, die prosedure asook die moontlike newe-effekte, wat relevant is vir die studie, is van kandidate - of indien die kandidate nie by magte was om toestemming te gee nie, van hul naasbestaandes verkry. Geskrewe toestemming is verkry. Indien die kandidate nie by magte is om self toestemming te gee en naasbestaandes nie beskikbaar was nie, is ingeligte toestemming telefonies van naasbestaandes verkry. Toestemmingsvorms was beskikbaar in Afrikaans, Engels and Suid-Sotho. Indien die kandidaat of naasbestaande nie Engels of Afrikaans magtig is nie, het ‘n geregistreerde verpleegkundige as tolk opgetree om die doel, prosedure en moontlike newe-effekte wat verband hou met die studie te verduidelik. ‘n Getuie het in alle gevalle die toestemmingsvorms geteken.

Een en sewentig kandidate, wat aan die insluitingskriteria voldoen het, is vir insluiting in die studie gesif. Vier en dertig van die kandidate was suksesvol in die studie ingesluit. Proefpersone is opeenvolgend in drie studiegroepe ingedeel. Elke spesifieke studiegroep is met die tipe endotrageale buis vir die spesifieke studiegroep geïntubeer, en bestudeer vir die ontwikkeling van ventilator-geassosieerde pneumonie. Die twee eksperimentele groepe het twee-uurlikse subglotiese suiging ontvang. Een eksperimentele groep se mansjetdruk is gemeet en binne die normale perke volgehou, terwyl 'n Lanz™ klep die ander eksperimentele groep se mansjetdruk beheer het. Die kontrole groep is met die konvensionele tipe endotrageale buis geïntubeer. Implementering het oor 'n tydperk van 18 maande plaasgevind.

Data is statisties geanaliseer en deur middel van frekwensies, mediane en vergelyking met 'n 95% vertrouensinterval voorgestel. Die studie het bevind dat geen van die kandidate in die eksperimentele groepe wat subglotiese suiging ontvang het, in vergelyking met die 16.67% in die kontrole groep, laat aanvang ventilator-geassosieerde pneumonie opgedoen het nie. Die insidensie van vroeë aanvang van ventilator-geassosieerde pneumonie was ook veel hoër (75%) in die kontrole groep as in die eksperimentele groepe. Die relatiewe risiko vir laat aanvang van ventilator-geassosieerde pneumonie dui aan dat subglotiese suiging nie 'n voorkomende strategie in die voorkoming van vertraagde intrede van ventilator-geassosieerde pneumonie in die eksperimentele groep was nie.

Die periode van intubasie van die kontrolegroep was langer as in die eksperimentele groepe. Geen merkwaardige verskille is in die morbiditeit en mortaliteit van die drie studiegroepe bevind nie.

Aanbevelings is dat 'n verlengde studie herhaal behoort te word en dat die proefpersone vir 'n langer periode geventileer behoort te word. Die voordele van subglotiese suiging behoort dan duideliker waarneembaar te wees. Die voordele van die Lanz™ klep is ook nie voldoende bestudeer in die studie nie.

As slotopmerking 'n paar wyse woorde:
"Keep an open mind toward pneumonia. Our grandchildren will be interested and are likely to have as many differences of opinion…as we have."
William Osler. 1900 (Craven & Steger, 1995:1S)

CHAPTER 1
RESEARCH DESIGN

1.1. INTRODUCTION

"Keep an open mind toward pneumonia. Our grandchildren will be interested and are likely to have as many differences of opinion…as we have."

William Osler. 1900 (Craven & Steger, 1995:1S)

When the patient is intubated "to save his life", the devices that invade the body, can cause complications and even death. The intensive care nurse has always been challenged with the prevention of ventilator-associated pneumonia, one of the major complications of intubation. Ventilator-associated pneumonia cannot totally be prevented, in spite of training in infection control principles and vigorous measures to implement these principles (Lynch, 2001:375S). A conclusion may be drawn that factors, other than the transgression of infection control principles, may be at play in the cause of ventilator-associated pneumonia, as it remains a problem in nursing practice. We should therefore look at new technology and procedures to address this problem. It is important that healthcare professionals should utilize all strategies to prevent the development of ventilator-associated pneumonia (Tasota, Fisher, Coulson & Hoffman, 1998:66).

Ventilator-associated pneumonia is divided into two groups, firstly early-onset pneumonia, within 48 to 72 hours after intubation, due to aspiration during intubation (Kollef, 1999:627). The second group is late-onset pneumonia occurring after 48 hours (Smulders, van der Hoeven, Weers-Pothoff & Vandenbroucke-Grauls, 2002:858). According to these authors, two processes have to take place for ventilator-associated pneumonia to develop, namely, bacterial colonization of the oropharynx and tracheobronchial tract and ensuing aspiration of these secretions to the lower respiratory tract.

1.2. PROBLEM STATEMENT

Ventilator-associated pneumonia is associated with high mortality, morbidity rates and medical costs (Smulders *et al.,* 2002:858). The incidence of ventilator-associated pneumonia is as high as 10% and 65% of all ventilated patients (Grap & Munro, 1997:419) but, depends on the group of patients being studied. The mortality rate of ventilator-associated pneumonia is the highest of all nosocomial infections. A crude mortality incidence of 59% to 71% is associated with ventilator- associated pneumonia, according to Ellstrom (1999:419) and the highest risk is within the first two weeks of mechanical ventilation.

Medical cost increase when patients develop a ventilator-associated pneumonia, due to the increased use of antibiotics and other medications, cross contamination of other patients and longer stay in the intensive care unit and hospital (Harris & Miller, 2000:51, 56). Although the price of endotracheal tubes facilitating subglottic suctioning is higher than the conventional endotracheal tubes, it is associated with a significant cost saving due to the high cost of ventilator-associated pneumonia (Shorr & O' Malley, 2001:232). Their study showed a saving of $11,400 per case in the prevention of ventilator-associated pneumonia.

Foreign objects like, amongst others, the endotracheal and the nasogastric tubes invade the body. The presence of both these devices attributes to the pathogenesis of ventilator-associated pneumonia (Kollef, Skubas & Sundt, 1999:1339). Both these devices are positioned in the oro-and/ or pharyngeal tract, causing an increase in oropharygeal secretions (Harris & Miller, 2000:56).

In informal research performed by the researcher, it was found that some cuffs leaked when a solution was dripped onto the cuff and some did not. The cuffs of different endotracheal tubes were inflated in a transparent tube similar to the size of the trachea. The cuffs differed in the way that they deployed in the trachea. Some cuffs had folds and some had none. These folds facilitated the leaking of the fluid past the cuff. The shape and the design of the cuff itself may attribute to micro-aspiration of

subglottic secretions.

New technology that needs further study is the endotracheal tubes that facilitate subglottic suctioning. Secretions from the maxillary sinuses, mouth, larynx and stomach accumulate on top of the cuff and can leak past the cuff to the lower respiratory tract (Harris & Miller, 2000:56). These secretions are usually contaminated with organisms that cause pneumonia, called ventilator-associated pneumonia.

Two of the endotracheal tubes that facilitate subglottic suctioning are the Hilo Evac™ (*Mallinckrodt, Athlone, Ireland*) endotracheal tube (see Figure. 1.1) and the Hilo Evac Lanz™ *(Mallinckrodt Medical, Athlone, Ireland)* endotracheal tube (see Figure 5.2). the Hilo Evac™ (*Mallinckrodt, Athlone, Ireland*) endotracheal tube has a suction catheter in the wall of the endotracheal tube that opens just above the cuff. Subglottic secretions can be aspirated through this catheter and therefore ventilator-associated pneumonia may be prevented. In addition, the Lanz™ valve, when inflated with 40 ml of air, maintains a cuff pressure of 30 to 34 cm H_2O.

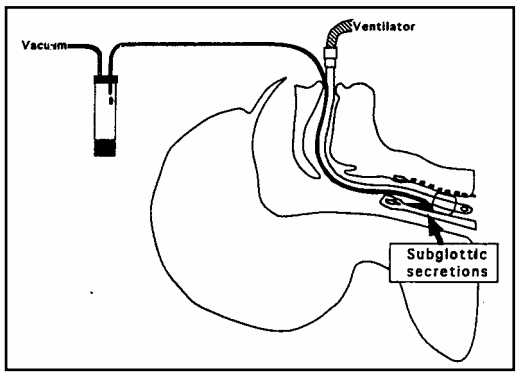

Figure 1.1: Endotracheal tube allowing for subglottic secretion suctioning (Vallès, Artigas, Rello, Bonsoms, Fontanals, Blanch, Frenándes, Biagorri & Mestre, 1995:180)

Positioning of the endotracheal tube is usually the responsibility of the physician, but it is primarily the function of the registered nurse to care for the endotracheal tube. These tasks will include the management of secretions, maintaining the position of the endotracheal tube, ensuring correct cuff pressures, prevention of complications and identifying and managing complications when they do occur.

1.3. AIM OF THE STUDY

The aim of the study is to determine the effect of three types of endotracheal tubes on ventilator-associated pneumonia.

1.4. OBJECTIVES

The research objectives are to compare three groups of subjects intubated with different types of endotracheal tubes regarding the:

a) incidence of ventilator-associated pneumonia;
b) risk factors;
c) causative organisms;
d) length of stay in intensive care;
e) cuff pressures;
f) morbidity; and
g) mortality.

1.5. CONCEPTUAL FRAMEWORK

The conceptual framework of the research is seen in Figure1.2. An explanation of the figure follows below.

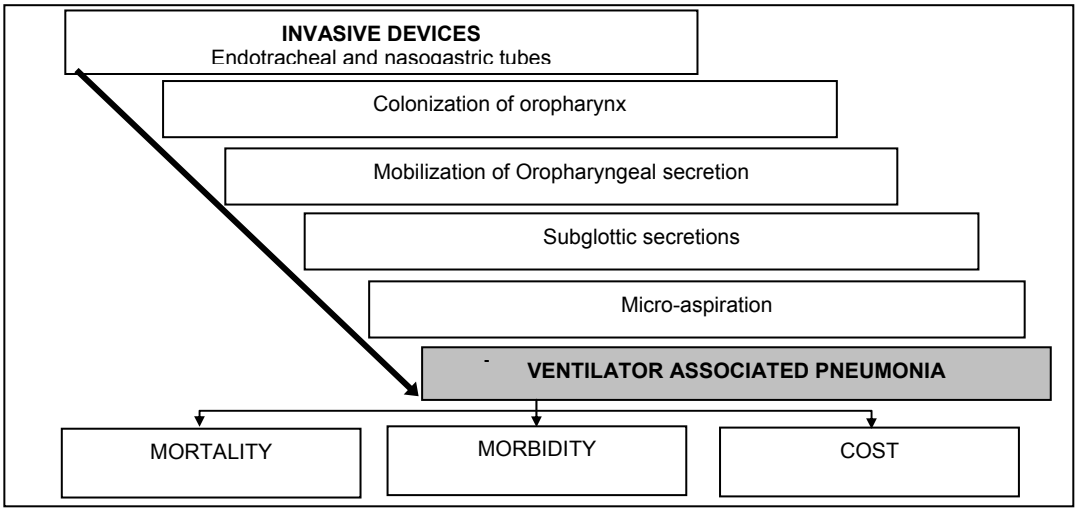

Figure 1.2: Development and consequences of ventilator-associated pneumonia

Intubation, the procedure that is supposed to save the patient's life, poses a risk to

the patient. The presence of the endotracheal tube reduces mucocillary function, causing ineffective cough mechanisms and bypass of other upper airway defence mechanisms. The endotracheal tube is also a foreign object in the oropharynx, causing excess secretion production. These excess secretions serve as a reservoir for the culture of organisms. These oropharyngeal secretions drain down the trachea and accumulate on top of the endotracheal cuff (Grap & Munro, 1997:420).

Nasogastric tubes are usually inserted through the nose into the stomach. Tubes inserted through the nose may even lead to sinusitis (Young & Ridley, 1999:1188). The nasogastric tube also makes swallowing uncomfortable and therefore oral secretions accumulate in the pharyngeal area. Movement of the nasogastric tube can even cause reflux of the gastric content (Young & Ridley, 1999:1191).

The nasogastric tube can acts as the “conductor” of organisms from the stomach to the oropharynx (Harris & Miller, 2000:56). The normal defence mechanisms cannot reach the organisms on the surface of the nasogastric tube, leading to colonization of the oropharynx. Bacterial colonization in the oropharynx is usually associated with nosocomial pneumonia (Grap & Munro, 1997:420; Vallès, *et al*., 1995:179).

The contaminated secretions drain down from the oropharynx and accumulate in the subglottic space on top of the endotracheal cuff (Harris & Miller, 2000:57). “The high-volume, low-pressure cuff of a tracheal tube does not prevent leakage of potentially infected fluid from the subglottis into the trachea" (Young & Ridley, 1999:1189).

In addition incorrect endotracheal cuff pressures attribute to leakage of secretions past the cuff and eventually to the development of ventilator-associated pneumonia. In the prevention of leakage of secretions past the cuff, cuff pressure cannot be inflated indefinitely. Cuff pressure should be maintained at 25-33 cmH_2O to ensure capillary perfusion of the inner wall of the trachea. Even with the use of high-volume, low-pressure cuffs a pressure of less than 34 cmH_2O is required (Boggs & Woodridge–King, 1993:44).

In a comparative study of 10 different endotracheal tubes, most endotracheal tubes demonstrated leaks around the cuff in vitro comparison at pressures of 40 cmH_2O. In the mentioned study, cuff pressure of the "second best type" of endotracheal tubes, cuff pressures were increased to higher than 50 cmH_2O to prevent leaking past the cuff. Pressures higher than $40cmH_2O$ kind reduce tracheal wall perfusion causing tracheal wall ischemia (Oikkonen & Aromaa, 1997:567).

The endotracheal tube moves during turning of the patient, as well as spontaneous movement, coughing, suctioning, etc. causing micro-aspiration of subglottic secretions. Restlessness (also associated with the neurosurgical patient) can also mobilize the subglottic secretions past the endotracheal tube's cuff. These secretions that leak past the endotracheal tube's cuff contaminate the otherwise sterile lower respiratory tract (Ellstrom, 1999:418).

The patient in the supine position is at higher risk of aspiration (Harris & Miller, 2000:56). The standard prescription for positioning of the post-operative neurosurgical patient is to nurse the patient's thorax at 20^o to 30^o in the supine position (Hickey, 1997:285, 320). This position may be insufficient to prevent aspiration because more than 45^o is generally recommended (Grap & Munro, 1997:422). The supine positioning of the patient during nursing management e.g. suctioning, bed washing, pressure area care, physiotherapy etc., is unavoidable. This may lead to further micro-aspiration of subglottic secretions that, which in turn leads to the development of ventilator-associated pneumonia.

The consequences of ventilator-associated pneumonia are related to an increase of morbidity, mortality and cost (Young & Ridley, 1999:1183) (see Fig 1.2). Morbidity figures range from 10% to 65%. The patient who develops a ventilator-associated pneumonia can develop acute respiratory failure in 9% to 24% of cases (Grap & Munro, 1997:419). Stay in Intensive care will be longer. The stay in the intensive care unit may extend up to 10 days longer (Grap & Munro, 1997:420). Complications

of ventilator-associated pneumonia include bloodstream infections and septic shock (Harris & Miller, 2000:51). Bloodstream infections and septic shock may further increase mortality rates. Literature regarding mortality figures varies, but these are on average between 54% and 71% (Grap & Munro, 1997:419).

The medical costs to the patient and the hospital increases due to morbidity that leads to increased medical stock use and antibiotic use. More medical and nursing staff are required in the care of these patients (Kollef, 1999:627). The increase in medical costs put more pressure on already limited resources in both public and private sectors.

Finally, subglottic suctioning prevents micro-aspiration and therefore contamination of the lower respiratory tract. Subglottic suctioning of secretions above the cuff can assist in reducing the mortality and morbidity of patients and in reducing costs to both the hospital and patient, when ventilator-associated pneumonia is prevented. The solution is to prevent ventilator-associated pneumonia rather than solving the problems associated with this disease.

1.6. RESEARCH METHODOLOGY

Under the heading of research methodology the following will be discussed, research design, population, sample and subject identification.

1.6.1. Research design

A single center, blind, prospective, controlled clinical trial has been selected to investigate the effect of three types of endotracheal tubes on ventilator-associated pneumonia. (See Figure 6.2 for the *Flow Diagram* of the research).

1.6.2. Population

The population is all candidates admitted to the Neurosurgical Intensive Care Unit of a tertiary public hospital in Bloemfontein, who are intubated in theatre before

neurosurgery, or require intubation in the Neurosurgical Intensive Care Unit and who meet that meets the criteria of the research.

1.6.3. Sample

A convenience sample will be drawn on the population admitted to the neurosurgical ward or Neurosurgical Intensive Care Unit of the research site. This group of subjects is selected on accessibility. The homogeneity of the group should be maintained and extraneous variables controlled.

The neurosurgeon will notify the researcher of prospective candidates for surgery, who are admitted to a public hospital in Bloemfontein who are expected to be ventilated for longer than 48 hours post-operatively. The researcher will visit the candidate in the ward; explain the purpose of the study and obtain informed consent.

If the candidate requires intubation in the intensive care unit and is unable to provide consent, the researcher will obtain consent from the candidate's family. If it is not possible to obtain consent before intubation (due to the urgency of the intubation), consent will be obtained from the candidate's family after intubation.

The subjects will be allocated consecutively to the study groups as indicated in the Table 1.1 below. Randomization of subjects would be a better method of allocation of study groups, but was not implemented, in order to prevent confusion of staff, because treatment procedures of the three study groups differ. Confusion regarding the procedures may lead to transgression of the research design and this may affect the reliability of the research. The reliability of the research will be affected if the staff becomes confused with procedures of the research.

Table 1.1: Allocation of subjects to study groups

GROUP ALLOCATION	NUMBER OF SUBJECTS	TYPE OF ENDOTRACHEAL TUBE
Group 1	22	HiLo™ Evac *(Mallinckrodt Medical, Athlone, Ireland).*
Group 2	22	HILO Evac Lanz ™ *(Mallinckrodt Medical, Athlone, Ireland).*
Group 3	22	Hi- Contour ™ *(Mallinckrodt Medical, Athlone, Ireland).*

Subjects of both Group 1 and 2 will receive subglottic suctioning. Group 3 will not receive subglottic suctioning, as this tube does not provide this function. The type of tube used in Group 3 is the standard for intubation at present and this group will serve as the control group. Groups 1 and 2 will be the experimental groups, as they will receive subglottic suctioning.

Each subject will be studied until the subject is extubated, undergoes a tracheotomy for a tracheostomy tube, passes away or meets the exclusion criteria. The morbidity and the mortality of the three groups will also be studied.

The sampling will commence in January 2003 and will continue until the quota of each group has been reached.

1.6.4. Subject identification

The identity of subjects participating in the study will be protected. Each patient will be identified with a number from 1-66. The subject's initials, surname and hospital number will be recorded against the research number on a *Record of subject details and study number* form (see Addendum 2). Only the researcher has access to this list.

1.6.4.1. Inclusion criteria

Candidates will be included in the study if they are:

a) age 18 years and older; and
b) expected to be intubated and ventilated for a period of longer than 48 hours.

1.6.4.2. Exclusion criteria

Candidates will be excluded from the study if they:

a) have a neutrophyl count of less than 1.6 X 10^9 /l (NHLS Laboratories Universitas Hospital values);
b) have a lymphocyte count of less than 0.6 X 10^9 /l (according to Professor P.J. Badenhorst Department of Haematology, UFS);
c) have experienced aspiration before or during intubation (aspiration before intubation will be suspected if chest X-ray indicates infiltration within the first 48 hours and no organisms are cultured of the first endotracheal aspirate);
d) are diagnosed with a pneumonia before intubation;
e) are expected to be ventilated for less than 48 hours;
f) used antibiotics at the onset of the study;
g) are intubated in another hospital, ward or intensive care unit than at the research site;
h) are diagnosed with primary lung cancer or other lung metastases;
i) are subjects in a clinical trail of a drug or device within 30 days prior to entering the trial;
j) are diagnosed with cystic fibrosis; or
k) are diagnosed with or suspected of tuberculosis.

1.6.4.3. Withdrawal criteria

The following incidences will lead to withdrawal of the subject from the research if:

a) Subject is extubated before 24 hours of mechanical ventilation

The subject who is ventilated mechanically for less than 24 hours does not provide enough information for this research and will be replaced with another subject. The

subjects ventilated for 24 to 48 hours will not be withdrawn, as they provide information regarding risk factors and causative organisms of early-onset ventilator-associated pneumonia.

b) Subject or the family requests withdrawal

The subject or the family has the right to request withdrawal from the study at any time. Should they request withdrawal, the subject will not be extubated. After withdrawal, the subject will still receive standard nursing care.

c) Subject accidentally extubates or self-extubates or requires re-intubation

The subject who accidentally- or self-extubates or requires re-intubation, will be re-intubated with the conventional endotracheal tubes available in the Neurosurgical Intensive Care Unit. These subjects will be withdrawn if the incident takes place before 24 hours of intubation. If it takes place after 24 hours the information up to the time of extubation will be utilized for research purposes. After withdrawal, the patient will receive the standard nursing care.

d) Subject is transferred to another intensive care unit or hospital

The subject who is transferred to another intensive care unit or hospital will be withdrawn from the research. The patient will not be extubated, but will not form part of the study any more. This subject will be replaced with another subject.

e) Death before 24 hours of intubation

Death before 24 hours of intubation will be considered as a withdrawal criterion. The subject will be replaced with another subject.

f) Are hypersensitive to cephalosporins, penicillins and to carbapenems

If the subjects are allergic to cephalosporins, penicillins and to carbapenems, requires these drugs for the treatment of a diagnosed ventilator-associated pneumonia and alternative therapy, will be withdrawn from the study.

Reasons for withdrawal of subjects from the study will be recorded and reported to the Sponsors.

1.6.4.4. Screening of candidates

Before screening the researcher will obtain informed consent as discussed under 1.7.1. After consent has been obtained, the subjects and replacement subjects will undergo screening for:

a) The presence of exclusion criteria

By completing the *Baseline information and final result f*orm (Addendum 4) exclusion criteria will be identified and these subjects will be excluded.

b) Presence of immune suppression:

Blood samples will be taken for full blood count result (5ml purple heparinized tube). This result will be evaluated for values that exclude the candidate from the research (see exclusion criteria 1.6.4.2).

c) Presence of pre-existing pneumonia:

Chest X-rays are usually taken preoperative. The blind investigator will evaluate the chest X-ray for the presence of pre-existing pneumonia. An endotracheal aspirate will be sampled within the first 6 hours after admission to the Neurosurgical Intensive Care Unit.

Criteria for pre-existing pneumonia are the same as for the ventilator-associated pneumonia and will be diagnosed by the blind investigator (see 1.9.2). The presence of these above-mentioned conditions will lead to exclusion.

Information regarding contact persons and telephone numbers will be obtained at this time. The presence of high risk factors will be obtained by interviewing the subject or a family member of the subject.

1.7. STUDY PERFORMANCE

A single centre, blind, prospective, controlled clinical trial (Spilker, 1987:144) will be utilized. The study site is a tertiary hospital, in a neurosurgical intensive care unit in Bloemfontein, South Africa.

A physician (as appointed by the sponsor) with the following qualifications M.BChB, M.Med (Int) and FCP (SA) will be the blinded investigator.

1.7.1. Informed consent

The researcher will visit the candidates before surgery or when identified for intubation and inform them, their spouse, child or parent (if the candidates are unable to provide consent) regarding the purpose, procedure, and possible adverse effects relevant to the study. Written consent will then be obtained. If the candidates are unable to give consent themselves and their family is unavailable, the researcher will obtain telephonic consent from above-mentioned family members (See Addendum 3 for *Consent* forms). The consent forms will be available in Afrikaans, English and South-Sotho. If the subject does not understand English or Afrikaans, the researcher will make use of a registered nurse as a translator to explain the purpose, procedure, and possible adverse effects relevant to the study. A witness must co-sign all consent forms.

After consent has been obtained, the subject will be screened for exclusion criteria. In the absence of exclusion criteria, the subject will be enrolled in the study.

1.7.2. Allocation to study groups

Sampling will commence January 2003. The subjects will be allocated consecutively to three groups comprising of 22 subjects each and will be studied for the development of a ventilator-associated pneumonia. Group 1 will be intubated with a HiLo^{TM} Evac *(Mallinckrodt Medical, Athlone, Ireland)* endotracheal tube. The next 22 subjects will be intubated with a HiLo Evac Lanz ^{TM} (*Mallinckrodt Medical, Athlone, Ireland*) endotracheal tube. The last 22 subjects will be intubated with the Hi-

Contour™ *(Mallinckrodt Medical, Athlone, Ireland)* endotracheal tube and be enrolled in Group 3. Both Group1 and 2 will receive subglottic suctioning. (See Addendum 1, Chapter 1 under heading 1.6 Specifications of endotracheal tubes.) The cuff pressures of Group 1 and 3 will be monitored.

The endotracheal tubes fall into the Class I group of devices, as they are least hazardous and are subjected to general controls like "good manufacturing practices, labelling, purity, banned devices, recalls record kept, and reports" (Spilker, 1987:141). The endotracheal tubes are also classified as Type II devices (topical devices) as they come in contact with the mucus membrane of the trachea (Spilker, 1987:142).

1.7.3. Intubation of the subjects

Intubation of the subjects could occur in theatre or in the Neurosurgical Intensive Care Unit. The management of the intubation may differ slightly, but the principles for intubation remain the same in the different departments.

1.7.3.1. Intubation in theatre

The researcher will provide the correct type of endotracheal tubes, according to the group assignment (see Table 1.1). The anaesthetist is responsible for the intubation of the subjects in theatre prior the neurosurgical procedure.

- The cuff pressure will be inflated to a pressure of 25 to 33 cmH_2O. During surgery it will be measured and recorded every 2 hours by the anaesthesia nurse.
- The anaesthesia nurse will also perform subglottic suctioning every 2 hours for 8sec. every 20sec. at a negative pressure of 100mgHg until all secretions are removed.
- Record of research procedures will be noted on the *Anaesthesia Report* form (Addendum 11).

1.7.3.2. Intubation in the Neurosurgical Intensive Care Unit

If intubation is required in thee Neurosurgical Intensive Care Unit, the subject will be intubated with the endotracheal tube of the current study group. (The applicable endotracheal tubes will be available in a separate marked box.) All the necessary equipment for mechanical ventilation will be available in the intensive care unit. After intubation and when the candidate is stabilized, the nursing staff will contact the researcher.

As it would not be able to obtain informed consent before intubation, the researcher will obtain consent from the subject's family. If consent cannot be obtained from the family or if the family does not give consent, the candidate will not be enrolled into the study, but will not be extubated. The candidate then receives the standard nursing care.

1.7.4. Management of the subjects

The following is the management of subjects after intubation.

1.7.4.1. Preparation of the ventilator

Either the researcher or the nursing staff will connect a disposable ventilator circuit and bacterial filters will be connected to the ventilator. Bacteria filters are connected to the inspiratory and expiratory leg of the circuit.

1.7.4.2. Nursing care of the subject on admission from theatre or after intubation

The subject receives the standard nursing care routinely performed on admission to the Neurosurgical Intensive Care Unit. The following extra duties should be performed after routine tasks have been completed and subject has been stabilized:

1) Disposable rectal thermometer will be inserted to measure core body temperature.
2) Closed multi-use catheter system will be connected before the first suctioning procedure.

3) At the time of the first suctioning procedure (within 6 hours after admission), an endotracheal aspirate sample will be collected in a Luki tube and immediately sent for microscopic analyses and sensitivity testing. If it is not possible to obtain an endotracheal sample, the sample will be collected at the next suctioning procedure.
4) Mobile chest X- rays will be taken in the Neurosurgical Intensive Care Unit in the anterior–posterior position. Distal end of endotracheal tube should be positioned 2 to 5 cm above the carina. The nursing staff or the neurosurgeon will evaluate the position of endotracheal tube post–operative. In case of incorrect position, subglottic suctioning will be performed in subjects of Group 1 and 2, cuff deflated and endotracheal tube correctly positioned. After repositioning, the cuff will be inflated to a pressure of 25 to 33 cmH_2O.

The *Daily Procedure* form (Addendum 5) will be available at the bedside of each subject. Performance of the research procedures will be recorded on the *Daily Procedure* form.

1.7.5. Daily nursing care of subjects

The subject will receive the standard nursing care routinely performed in the Neurosurgical Intensive Care Unit. The following research procedures should be performed (also see *Standard Operating Manual,* Chapter 4 in Addendum 1):

1) The **cuff pressures** are measured every two hours. The nursing staff ensures that cuff pressure is maintained between 25 and 33 cm H_2O. The cuff pressures will be recorded on the *Daily Procedure* form (Addendum 5).
2) The subject will be **positioned** in 20-30^0 or according to the prescription of the Neurosurgeon.
3) Subjects will receive routine **endotracheal suctioning,** when peak airway pressure on the ventilator increases, when secretions are audible or visualized. The physiotherapist or the nursing staff will perform the suctioning procedure. (Subglottic suctioning should be performed before every suctioning procedure.)

The closed multi-use catheter system will be utilized for the suctioning procedure. The physiotherapist will change the closed multi-use catheter system daily. The procedure will be recorded on the *Daily Procedure* form (Addendum 5) with a ✓. The physiotherapist or nursing staff will classify the appearance of the secretions on the procedure form.

4) **Subglottic suctioning** will be performed intermittently every two hours for 8sec. every 20sec (Smulders *et al*., 2002:859) at a pressure of 100mgHg until all subglottic secretions are removed. This procedure may be performed more frequently if deemed necessary. Performance of this procedure will be recorded on the *Daily Procedure* form (Addendum 5) by indicating it with a ✓. This method, instead of continuous subglottic suctioning, was selected to prevent drying out the tracheal wall.
5) Every Monday and Thursday morning a **full blood count** will be taken in a 5ml purple heparinized tube by the night staff. The nursing staff will indicate on the *Daily Procedure* form (Addendum 5) when the sample was taken by indicating it with a ✓.
6) Every Monday and Thursday the physiotherapist will collect an **endotracheal aspirate** in a Luki tube for microscopic analyses and sensitivity testing. The physiotherapist will indicate it with a ✓ on the *Daily Procedure* form (Addendum 5) when the sample was taken.
7) Daily **chest X-ray** will be taken with a mobile unit. The nursing staff will indicate it with a ✓ on the *Daily Procedure* form (Addendum 5) when the sample was taken.
8) The **disposable ventilator circuits** and bacterial filters will be changed every 7 days. This will be the responsibility of the physiotherapist. This procedure will be indicated on the *Daily Procedure* form (Addendum 5) with a ✓.

1.8. PILOT STUDY

A pilot study that includes three subjects will be performed in the beginning of January 2003. The subjects will be intubated with the tube of Group I. The purpose of the pilot study is to evaluate if the nursing staff comply with the suctioning procedure, cuff pressure monitoring, subglottic suctioning procedures and recording

of data.

A further purpose of the pilot study is to ensure that the researcher is familiar with the screening of the subject's baseline assessment. The *Baseline Information and final result* (Addendum 4) and *Daily Procedure* forms (Addendum 5) will also be evaluated for insufficiencies.

1.9. MEASUREMENT AND DATA COLLECTION

The researcher will interview the candidate or the family to obtain the necessary information to complete the B*aseline information and final results* (Addendum 4) and the *Daily activity assessment* form (Addendum 7) after screening the subject. Data regarding the intubation of the subject will be collected on the *Anaesthesia Report* and *Intubation in the Neurosurgical Intensive Care Unit* form (Addendum 11). Data during the stay in the intensive care unit will be recorded on the *Daily Procedure* form (Addendum 5). Results regarding the diagnosis of ventilator-associated pneumonia will be recorded on the *Information for Blind Investigator regarding diagnosis of ventilator-associated pneumonia* form (Addendum 6). Finally, the *Daily activity assessment* form (Addendum 7) will be completed at day 42. The collection of data is summarized in the Table1.2. The table compares the data to be collected, the addendum that it appears in, number of the element in the table and the objective of the study that it meets. The lines that are left open does not relate directly to any research objective. An explanation of the elements that require more clarification will follow.

Table 1.2: Instruments for data collection

INFORMATION	NUMBER OF ADDENDUM	NUMBER IN ADDENDUM	RESEARCH OBJECTIVE
DEMOGRAPHIC INFORMATION			
Date of assessment	4	1.1	
Surname, initials and study number		1.2 and 1.3	
Hospital number		1.5	
Gender		1.6	
Age		1.7	Risk factors
Neurosurgical diagnosis or surgical procedure		1.8	Risk factors
SCREENING DATA			
Lymphocytes	4	4.1	Risk factors
Leucocytes		4.2	Risk factors
Neutrophyls		4.3	Risk factors
Chest X-ray infiltration before 48 hours		4.4	Incidence of ventilator-associated pneumonia
Positive endotracheal aspirate culture and sensitivity test result		4.5	Causative organism
PRE-INTUBATION RISK FACTORS			
Medical conditions	4	1.9	Risk factors
Previous surgical history		1.10	Risk factors
Trauma in past two weeks		2.1	Risk factors
Chronic obstructive pulmonary disease		2.2	Risk factors
Smoking presently		2.3	Risk factors
Diabetes mellitus		2.4	Risk factors
Medications suppressing immune system Previous frequent antibiotic use Steroid therapy H_2- antagonists		2.5	Risk factors
Suppression of level of consciousness		2.6	Risk factors
Malnutrition		2.7 and 7.1-7.4	Risk factors
Present antibiotic use		4.6	Risk factors
Diagnosed pathology of: Lung cancer Suspected lung metastasis Cystic fibrosis Suspicion of, or actual tuberculosis		 4.8 4.9 4.11 4.12	Risk factors
GENERAL INFORMATION			
Subject in any trial in past 30 days	4	4.10	
Daily activity assessment (Barthel index) (at screening and 42 days)	7	1-10	Morbidity
Location at 42 days	7	11	Morbidity
Date and time of extubation	4	5.1 and 5.2	Morbidity
Hours ventilated	4	5.3	Morbidity
Type of ventilator	4	5.4	
Number of days in intensive care unit	4	5.5	Length of stay in the intensive care unit

INFORMATION	NUMBER OF ADDENDUM	NUMBER IN ADDENDUM	RESEARCH OBJECTIVE
Date transferred to ward	4	5.6	Length of stay in the intensive care unit
Date of discharge	4	5.7	Morbidity
Withdrawal criteria	4	4.1 and 4.2	
Date of death	4	6.1 and 6.2	Mortality
Date and cause of death	4	6.1 and 6.2	Mortality
INTUBATION DATA			
ANAESTHESIA REPORT			
Date	11.1	1	
Time of intubation		2	
Time of end of anaesthesia		3	Risk factors
Subglottic suctioning performed		4	
Cuff pressure monitoring		4	Cuff pressures
Aspiration suspected		5	Risk factors
Position during anaesthesia		6	Risk factors
Duration of anaesthesia		7	Risk factors
INTUBATION IN NEUROSURGICAL INTENSIVE CARE UNIT			
Date	11.2	1	
Time of intubation		2	
Information of physician that intubates		3	Risk factors
Aspiration suspected		4	Risk factors
Route of intubation		5	Risk factors
POST-INTUBATION RISK FACTORS			
Nasogastric tube	5	9.1	Risk factors
Intracranial pressure device		9.2	Risk factors
Level of consciousness		9.3	Risk factors
Immunosuppresive drugs		9.4	Risk factors
Enteral feeding		9.6	Risk factors
Bronchoscopy		9.7	Risk factors
Nebulization		9.8	Risk factors
H_2-antagonists use		9.9	Risk factors
POST-INTUBATION RISK FACTORS			
Nasogastric tube	5	9.1	Risk factors
Intracranial pressure device		9.2	Risk factors
Level of consciousness		9.3	Risk factors
Immunosuppresive drugs		9.4	Risk factors
Enteral feeding		9.6	Risk factors
Bronchoscopy		9.7	Risk factors
Nebulization		9.8	Risk factors
H_2-antagonists use		9.9	Risk factors
POST-INTUBATION PROCEDURES			
Subglottic suctioning	5	1	
Endotracheal tube cuff pressure		2	Cuff pressures
Closed suctioning procedure		3	
Mouth care		4	
Temperature record		5	
Investigations performed Full blood count Endotracheal aspirate Daily chest X-ray		6	

INFORMATION	NUMBER OF ADDENDUM	NUMBER IN ADDENDUM	RESEARCH OBJECTIVE
Record of changing of: Closed multi-use catheter system Ventilator circuit Inspiratory and expiratory bacterial filters		7	
Antimicrobial therapy use		8.1-8.4	
Was antimicrobial therapy for ventilator-associated pneumonia?		8.4	
DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA			
Leukocytes	6	2.1.1	Incidence of ventilator-associated pneumonia
Endotracheal aspirate cultures Organism cultured Sensitive antibiotic Resistant antibiotic		2.2	Causative organism
Is ventilator-associated pneumonia present?		2.3 and 3.2	Incidence of ventilator-associated pneumonia
Date of ventilator-associated pneumonia		2.4	Incidence of ventilator-associated pneumonia
Type of ventilator-associated pneumonia		2.5	Incidence of ventilator-associated pneumonia
INTERPRETATION OF CHEST X-RAYS			
Result of chest X-ray	6	3	Incidence of ventilator-associated pneumonia

1.9.1. Baseline information (Addendum 4):

The following information will be obtained from the patient or his family after informed consent has been obtained.

1.9.1.1 Demographic information

The demographic information list in Table 1.2 will be collected by completing Addendum 4.

1.9.1.2. Risk factors

Risk factors are divided into pre-intubation and post-intubation risk factors. Pre-operative risk factors will be recorded in Addendum 4. Post-operative risk factors will be recorded on the *Daily Procedure* form (Addendum 5). Below is a description of the method of data collection of the risk factors that need clarification.

Suppression of level of consciousness

Suppressed level of consciousness is characterized by the lack of orientation according to time, place and person. The researcher will ask questions of which the answers can be verified such as, what day of the week, what season of the year, which hospital is this and name your children (if they are present). The situation will determine the type of questions that can be asked.

MaInutrition

The nutritional status will be assessed by means of anthopometrical measures. The subcutaneous fat (skinfold thickness) and skeletal muscle size will be assessed. The following skinfold thickness will be measured: the triceps skinfold thickness and the subscapular skinfold thickness (Mahan, 1996:954). The sum of the two values will be compared with the percentile in Appendix 8. Skeletal muscle size will be determined by measuring the mid-upper arm circumference. The arm muscle circumference is a good indicator of protein nutrition (Hickey, 1997:170). The results will be compared with percentiles of the particular age and gender (Frisancho, 1999:22,87,90,103,106) (Addendum 8).

1.9.2. Information for blind investigator regarding diagnosis of ventilator-associated pneumonia (Addendum 6)

The researcher will supply the blind investigator with documents containing below mentioned information for the diagnosis of ventilator-associated pneumonia. The results will be recorded on the *Information for blind investigator regarding diagnosis of ventilator-associated pneumonia* form (Addendum 6).

1.9.2.1. Laboratory results (Addendum 6)

a) Full blood count will to identify the presence of leucocytosis (a count >$10x10^9$ /L), neutrophilia (1.6 X 10^9 /l) and lymphocytopenia (0.6 X 10^9 /l). According to Professor P.J. Badenhorst of the Hematology Department of the University of the Free State, for the purposes of this study it is sufficient to observe these three values to identify suppression of the immune system or the presence of an infection. The decision was made due to the cost and ethical considerations

involved in performing an HIV test or CD_4 count.

b) Microscopic cultures and sensitivity testing of endotracheal aspirates will be performed to identify pathogens and possible treatment. (The organisms cultured, with their sensitivities and resistance, will be recorded.) When the laboratory results indicate that the cultured organism is a contaminant, the result will not be considered as relevant to research data.

1.9.2.2. Daily procedure form (Addendum 5)

The person performing the endotracheal suctioning will record it after each procedure and the appearance of the endotracheal secretions will be recorded on the *Daily Procedure* form (Addendum 5). Any description of secretions that is not clear, will be considered as purulent for research purposes.

1.9.2.3. Temperature monitoring

Rectal temperature will be recorded every 2 hours and measured in ^{o}C. Nursing staff will record the temperature on the *Daily Procedure* form (Addendum 5) observation chart. The researcher will provide these results to the blind investigator.

Pyrexia is one of the criteria for ventilator-associated pneumonia and will be considered at a rectal temperature higher than 38, 3 ^{o}C (Cook, Jonghe, Brochard, & Brun-Buisson, 1998:783).

1.9.2.4. Chest X-ray

A chest X-ray will be taken on admission and after that on a daily basis. The chest X-ray will be collected and provided together with the *Information for the blind investigator regarding the diagnosis of ventilator-associated pneumonia* form (Addendum 6). The blind investigator should evaluate each chest X-ray for new or progressive infiltration or cavitation. He will then determine whether ventilator-associated pneumonia is present or not, after having considered all information provided and record it on the *Information for blind investigator regarding diagnosis of ventilator-associated pneumonia* form (Addendum 6).

1.9.2.5. Morbidity

Monitoring the number of days spent in the Neurosurgical Intensive Care unit as well as the number of hours ventilated, number of days spent in the hospital assesses morbidity. At the 42nd the researcher will contact the subject and record the location at 42 days.

The presence of morbidity will influence the subject's ability to care for themselves called daily activities. These daily activities will be assessed at screening and after 42 days by means of the Barthel index (Mahoney & Barthel, 2002:1) (Addendum 7). The more a subject is challenged, the lower the score on the Barthel Index.

It is the normal practice in other studies to obtain this information after 28 days, but in this research's population, it may be impossible to make personal or telephonic contact with the subjects at the relevant time. Neurosurgical patients are usually seen again by the neurosurgeon at outpatients department six weeks (42 days) after the operation. The researcher has therefore selected the 42-day period for the evaluation of activities of daily living and the care the subject requires at this time.

The score of the Barthel index at screening and at 42 days after commencement will be compared when analyzing the data.

1.9.2.6. Mortality

Mortality will be assessed according to date of death and the major cause thereof. This information will be obtained from nursing records, laboratory results, death certificates, records of the neurosurgeon or by contacting the family. The data will only be followed up until 42 days after the operation.

1.9.2.7. The blind investigator

The sponsor will appoint the blind investigator. The researcher will provide the blind investigator with the information necessary to make the diagnosis. The blind investigator is responsible for interpretation of the chest X-rays, laboratory data, temperature of the subject and appearance of secretions. After consulting previously

mentioned data the diagnosis of ventilator-associated pneumonia will be made. If present, the pneumonia will be classified as early- or later-onset ventilator-associated pneumonia. The blind investigator is not allowed to see the subject.

The blind investigator is also responsible for drawing up guidelines for the treatment of a ventilator-associated pneumonia in subjects of this study. The guidelines will ensure that the subject who develop ventilator-associated pneumonia, do receive effective antimicrobial therapy. Improper management may have unwanted negative effects on the morbidity and even on mortality.

A second blind investigator will be appointed for circumstances where the first blind investigator is not available. The second blind investigator should adhere to the prescription of antibiotics by the first blind investigator.

1.10. VARIABLES AND THE CONTROL THEREOF

Variables will be divided into dependent and independent variables.

1.10.1. DEPENDANT VARIABLES

"Dependant variable is the response, behaviour or outcome the researcher wants to predict or explain" (Burns & Grove, 1997:186). In this research the following dependent variables have been identified.

1.10.1.1. Colonization

Colonization is the presence and growth of an organism, but it does not penetrate the tissue. The organ is therefore not exposed to the toxins of the organism. Organisms can colonize on the oropharynx, skin, colon, vagina and surfaces of wounds (Reese & Betts, 1996:946-947).

Oropharyngeal colonization

Oropharyngeal secretions are the secretions that have their origin in the mouth, nose or pharynx of the patient. The normal flora of the oropharynx prevents gram-negative organisms and other pathogens from colonizing. When the normal flora is destroyed

by the use of antibiotics, colonization of gram-negative organisms and other pathogens occur. Contaminated oropharyngeal secretions drain down the trachea and accumulate in the subglottic space above the cuff of the endotracheal tube (Harris & Miller, 2000:56).

Gastric colonization

Gastric content is usually sterile due to the presence of hydrochloric acid. The use of H_2-antagonists, antacids, and enteral feeds may increase the pH of the stomach. These factors increase the risk for colonization of pathogens in the stomach. Reflux of gastric content into the oesophagus is caused by an increased volume and pressure in the stomach. This reflux attributes to the colonization of gram-negative organisms and other pathogens in the oropharynx (Harris & Miller, 2000:54). Gastric content can also drain down the trachea and accumulate in the subglottic space above the cuff of the endotracheal tube cuff (Kollef, 1999:627).

Micro-aspiration

Micro-aspiration takes place into the lower respiratory tract when subglottic secretions, composed of oropharyngeal secretions and/or gastric content, leak past the cuff of the endotracheal tube into the lower respiratory tract (Grap & Munro, 1997:421).

1.10.1.2. Ventilator-associated pneumonia

Ventilator-associated pneumonia is a type of pneumonia that occurs in patients receiving mechanical ventilation. Ventilator-associated pneumonia is usually divided into two groups, early-onset ventilator-associated pneumonia and late-onset ventilator-associated pneumonia.

Early-onset ventilator-associated pneumonia develops within the first 48 hours of ventilation. This is not a true ventilator-associated pneumonia, as the cause is a community-acquired pneumonia. Subglottic suctioning will not have any effect on early-onset ventilator-associated pneumonia (Smulders *et al*., 2002:861).

A late-onset ventilator-associated pneumonia is not present at the moment of intubation, but develops after 48 hours. The inner lumen and the outer surface of the endotracheal tube serve as a route for organisms to the lower respiratory tract and facilitate colonization of organisms (Grap & Munro, 1997:419) in and around the tube itself.

The blind investigator will differentiate between early and late-onset ventilator-associated pneumonia.

Diagnosis of ventilator-associated pneumonia is made when:

The diagnosis of a ventilator-associated pneumonia will be made in the presence of:

1) new progressive infiltration seen on chest X-ray; and
2) positive endotracheal aspirate culture of a pathogen, associated with:
3) purulent endotracheal secretions observed during suctioning; and
4) pyrexia (rectal temperature of $\geq 38{,}3^0$C) or hypothermia (rectal temperature of $< 36^0$C) or leucocytosis of $>10x10^9$ /L (Cook, *et al*., 1998:783; Young & Ridley,1999:1184).

The results of laboratory tests, temperature, and the chest X-ray will be provided to the blind investigator to make the diagnosis of ventilator-associated pneumonia.

The blind investigator will draw up guidelines for the prescription of antibiotics for subjects of the study, in case of a ventilator-associated pneumonia. The guidelines will be available at the bedside of the subject. If the neurosurgeon deems it necessary to prescribe another type of antibiotic, must first consult with the blind investigator.

1.10.1.3. Intubation period

The intubation period is the period from the first hour of intubation (in theatre) till the hour of extubation or death. The period of intubation will be measured in hours.

1.10.1.4. Antimicrobial therapy

Antimicrobial agents are prescribed according to the results of the microbiology culture and sensitivity testing (Grap & Munro, 1997:425). In the case the microbiological culture and sensitivity cultures are not available, an empiric decision is made to determine the causative organism. The neurosurgeon will prescribe the antimicrobial therapy according to the guidelines set by the blind investigator.

1.10.1.5. Bacterial organisms

Bacterial organisms are unicellular micro-organisms that invade the body and cause disease (Reese & Betts, 1996:258).

1.10.2. Independent variables

The independent variable is the stimulus or activity that is manipulated or varied by the researcher to create an effect on the dependent variable (Brink, 1996:93). The following are the independent variables of this research.

1.10.2.1. Intubation with three different types of endotracheal tubes

In this study subjects will be intubated with one of three kinds of endotracheal tubes: Hi- Contour ™ (*Mallinckrodt, Athlone, Ireland*) endotracheal tube, HiLo Evac™ (*Mallinckrodt, Athlone, Ireland*) endotracheal tube and the HiLo Evac with the Lanz™ valve **(***Mallinckrodt, Athlone, Ireland*) endotracheal tube (see specifications of types of endotracheal tube in Addendum 1).

Oral or nasal intubation may be used. The anaesthetist will intubate subjects in theatre with the size of endotracheal tube of his choice provided by the researcher according to the allocation of study groups. In some circumstances the neurosurgeon may need to intubate subjects in the Neurosurgical Intensive Care unit. The endotracheal tubes of the study group will be available in the unit.

After intubation the endotracheal tube will be secured with plaster, applied around the head and around the endotracheal tube (see Standard Operating Procedure 4.2.2.3 for the pattern of plaster securing the endotracheal tube).

1.10.2.2. Intubation of subjects by the anaesthetists (rotating monthly)

Before surgery the anaesthetist will be issued with the three different sizes (7.5, 8.0 and 8.5) of the type of endotracheal tube for the applicable study group. Although the techniques of intubation may differ, the same basic principles will apply. The sponsor will explain the inflation of the cuff of the endotracheal tube in the training session of the anaesthetist and the anaesthesia nurse. The anaesthesia nurse will be supplied with a cuff pressure-monitoring device and should keep the cuff pressures between 25-33 cm H_2O. The anaesthesia nurse will measure cuff pressures every two hours during surgery. The anaesthesia nurse will also apply subglottic suctioning every 2 hours.

1.10.2.3. Intubation of subjects by the neurosurgeons in the Neurosurgical Intensive Care Unit

The subject who requires intubation in the Neurosurgical Intensive Care Unit will be intubated by the neurosurgeon on call. There are in total seven neurosurgeons and clinical assistants in the Neurosurgical department. The neurosurgeon will intubate the subject with the endotracheal tube for the applicable study group. The researcher will make a size 7.5, 8.0 and 8.5 available in a marked box on the emergency trolley. If the subject is intubated in the Neurosurgical Intensive Care Unit, the same procedure will be followed as on admission from theatre.

1.10.2.4. Nursing staff and intensive care students

Some of the nursing staff and intensive care students rotate each month. To ensure that the new nursing staff is trained in the management of the subjects, the training will be repeated each month for the rotating staff.

1.10.2.5. Ventilator aspects

Ventilator aspects that will be discussed is type of ventilator, settings, circuits, endotracheal suctioning and endotracheal aspirate sampling, humidification, bacterial filters, subglottic suctioning and cuff pressures.

Type of ventilator

The Puritan Bennett 7200 and the Newport Wave model E200 will be utilized in the study. The nursing staff will determine the ventilator used according to availability of ventilators.

Ventilator settings

The mode of ventilation will be synchronized intermittent mandatory ventilation and the type of ventilation will be volume-controlled ventilation.

- The tidal volume will be calculated according to the formula of 6-8ml x body weight in kilograms.
- The frequencies of ventilation will commence with ten rates per minute. The rates will be adjusted according to the bloodgas results or patient condition. The rates will be weaned down by two rates per minute until 4 rates are reached. The patient will then be put on spontaneous breathing.
- The FiO_2 at 0,40 and will be changed according to the bloodgas results or patient condition.
- A pressure support of 8 cm H_2O is usually applied.
- Peak-flow setting may vary between 40 to 60 L/min.
- Changes will be made to settings according to the bloodgas results and/or patient's condition. All changes to the ventilator will be made according to the subject's bloodgas result.

Ventilator circuits

Disposable ventilator circuits will be used in the research. The circuits will be changed every 7^{th} day or when the circuit is visibly soiled. Changing of disposable circuits will be recorded on the *Daily Procedure* form (Addendum 5).

Endotracheal suctioning and endotracheal aspirate sampling

Closed multi-use catheter system suctioning will be used during the suctioning procedure, to exclude the possibility of contamination. The closed multi-use catheter system will be connected to a Gabler high vacuum suction device. The patient will be pre-oxygenated before the suctioning procedure with 100% oxygen. The patient is

ventilated with the manual button on the ventilator during the suctioning procedure. The use of the resuscitation-bag in the endotracheal suctioning procedure is not recommended for neurosurgical patients, as it increases intra-cranial pressure.

The physiotherapist will change the closed multi-use catheter system daily or when blocked. Routine suctioning of the subject will be recommended, but more frequent suctioning may also be required. Procedure will be performed by the nursing staff or the physiotherapist and recorded on *Daily Procedure* form.

As the closed multi-use catheter system will be changed daily, an endotracheal aspirate sample will be collected in a Luki tube after the suction catheter is changed. The physiotherapist will be responsible to obtain the endotracheal aspirate in an aseptic manner.

Humidification

The Respiratory Humidifier Fisher and Pagal MR 700 humidification system will be used and all temperatures will be set at 39 ^{O}C. A 1-litre bag of sterile water for irrigation will be connected to the humidification system and replaced when empty. This will ensure that secretions will be humidified and will also prevent blocking of endotracheal tubes.

Bacterial filters

Every 7th day the physiotherapist will change the inspiratory and expiratory filters as the circuit will be also be changed.

Subglottic secretions

Subglottic secretions develop by means of oropharyngeal secretions draining down the trachea and gastric content that reflux into the oesophagus eventually draining down the trachea. These subglottic secretions accumulate above the cuff of the endotracheal tube in the subglottic space (Harris & Miller, 2000:57).

Cuff pressure

Cuff pressure is the pressure in the endotracheal tube cuff after inflation with air. The cuff pressure of the patients intubated with the Hi- Contour ™ (*Mallinckrodt, Athlone, Ireland*) endotracheal tube and the HiLo Evac™ (*Mallinckrodt, Athlone*, *Ireland*) endotracheal tube will be measured and maintained between 25 and 33 cmH_2O. Boggs and Woodridge-King (1993:44) recommend a pressure of 25 to 34 cmH_2O, but the Lanz valve provides a pressure of 25 to 33 cmH_2O and therefore this pressure was selected. Cuff pressure monitoring of the HiLo Evac™ (Mallinckrodt, Athlone, Ireland) endotracheal tube with Lanz valve is not necessary as the valve maintains the pressure in the cuff automatically. Cuff pressures will be measured with a HiLo™ cuff pressure manometer.

1.11. TRAINING OF RELEVANT PARTIES

The training of the following parties will be discussed: the anaesthetist and anaesthesia nurse, the nursing staff and physiotherapists and the neurosurgeons.

1.11.1. Training of the anaesthetist and anaesthesia nurse

All the anaesthetists and anaesthesia nurses will be invited for tea in the theatre tearoom. The purpose, method of and their role in the research will be explained. The differences in the endotracheal tubes will be demonstrated and the benefits explained. Measuring of cuff pressures will also be demonstrated at this time.

Intubation can either be performed through the mouth or nose. Aseptic techniques and the prevention of aspiration will be emphasized. The endotracheal tube must be positioned in the trachea, 2-5cm above the carina. On intubation the anaesthetist must ensure that both lungs are ventilated. The cuff pressure must be inflated to 25 to 33 cmH_2O. In case of the HiLO Evac™ endotracheal tube with the Lanz™ valve, the cuff is inflated with 40 ml of air.

Subglottic suctioning will be preformed every two hours or when deemed necessary more frequently during surgery. The suctioning will be applied for 8sec. every 20sec at a pressure of 100mgHg. The subglottic suctioning procedure and cuff pressure

monitoring will be recorded on the *Anaesthesia Report* form (Addendum 11).

The research design and Standard Operating Procedure (Addendum 1) will be made available to the neurosurgical theatre, in case of further questions. The researcher's telephone number is also available when problems are experienced.

1.11.2. Training of nursing staff and physiotherapists

A workshop will be held in the tearoom of the Neurosurgical Intensive Care unit. The researcher and the sponsor will present an information session on the purpose of the research. A demonstration of the function, differences and management of the endotracheal tubes will be given. Oral care of the patient will be emphasized and should be performed every 6 hours. The Standard Operating Manual Procedure (Addendum 1) of the research will be available at the bedside of each subject. After the training session, tea and cake will be provided.

1.11.3. Training of the Neurosurgeons.

The researcher and sponsor will present at a workshop for the neurosurgeons. The purpose, objectives, inclusion and exclusion criteria of the research will be explained. A demonstration of the different types of endotracheal tubes and the management thereof will be presented. The importance of the identification of candidates will be emphasized. The procedure of notifying of the researcher regarding candidates will be explained.

The patient developing pneumonia receives the standard care. The Neurosurgeon prescribes the antibiotic according to the guidelines drawn up by the blind investigator. If it is necessary to prescribe another antibiotic, the neurosurgeon should first discuss it with the blind investigator.

1.12. VALIDITY AND RELIABILITY

Below is a discussion of the measures taken to increase the validity of the study.

- A similar study is at present being performed in the Netherlands and the researcher will be in contact with these researchers for information on their

research methodology. This will increase the validity of this research, as the subject is of present extensively researched.

- The subject of study was selected due to the problems experienced in the practical setting with the development of ventilator-associated pneumonia.

Below is a discussion of the measures taken to increase the reliability of the study.

- The researcher will manage the data herself. A monitor and an auditor will check the data.
- An independent blind investigator, qualified in internal medicine and currently busy with his studies as an intensivist, will make the diagnosis of a ventilator-associated pneumonia. (His studies were successfully completed by the end of this research). A second blind investigator will be appointed in case of unforeseen problems. This investigator is the consultant at the Critical Care Department of the Faculty of Health Sciences of the University of the Free State.
- The diagnosis of the ventilator-associated pneumonia is based on objective results from laboratories, calibrated monitors, and chest X–rays. The diagnostic criteria are according to acceptable guidelines based on a study of literature.
- Data recorded will be checked for correctness by a monitor and auditor appointed by the sponsor.
- Calibration of monitor measuring the subject's temperature, the manometer taking the cuff pressures and the calliper, will be effected before the commencement of the study and after that every six month.

The researcher's telephone number will be available at the Neurosurgical Intensive Care Unit if problems are experienced.

1.13. ADVERSE EVENTS

The researcher, the nursing staff and the Neurosurgeon will monitor each subject for an adverse event. Any suspected or proven adverse event will be reported to the researcher by noting it on the study procedure record.

In the case of an adverse event, the researcher will decide with her study leader and the neurosurgeon if the subject will be withdrawn from the study. The Ethics Committee, and the sponsor will be notified in case of such an event by E-mail. The researcher will draw up a report of the date, time, nature, steps taken, study device involved and outcome of each event.

In a study by Kollef *et al*. (1999:1343) performed on patients who had undergone cardiac surgery, no adverse effects were experienced.

1.14. ANALYSIS OF DATA

Demographic and baseline information will be summarized per group. Medians and percentiles will summarize numeric variables as the distributions are skewed. Categorical variables will be summarized by frequencies and percentages. Changes between baseline and consecutive treatment week information will be summarized per group by medians and percentiles or percentages as appropriate, and described by means of 95% confidence intervals for the difference between groups.

Changes in daily activities from baseline to 42 days will be calculated within and between groups and will be compared by means of 95% confidence intervals for the percentage difference.

1.15. ETHICAL ASPECTS AND GOOD CLINICAL PRACTICE COMPLIANCE

Permission for the research will be obtained from the:

- Ethics Committee of the Faculty of Health Science;
- hospital management;
- manager of the Intensive Care Units;
- physician in charge of the Neurosurgical Department of the University of Free State; and
- registered nurse in charge of the Neurosurgical intensive care unit.

Consent for inclusion in the study will be obtained from the patient or the family and they will be informed of:

- purpose of the research;
- possible complications or side–effects;
- subglottic suctioning as an additional action to normal nursing care ;
- the fact that the researcher will contact the subject in about 42 days to complete a questionnaire and to ascertain general state of mind; and
- confidentiality will be maintained at all times.

The participation of the subjects is voluntary and they may withdraw whenever desired. There will be no cost involved to the patient regarding the study, but remuneration for participation will not take place.

The patient or the family will sign an informed consent form. In case of a disorientated patient and absence of family, the primary investigator will attempt to obtain telephonic consent, signed by a witness of consent given.

1.16. RESEARCHER'S OBLIGATIONS

The researcher's responsibility is to:

- apply the research design and ensure adherence thereto by all parties;
- monitor and report adverse events;
- supply products related to the research;
- collect and record data; and
- train participants.

1.17. SPONSOR'S OBLIGATIONS

The sponsor's obligations are to provide the following products on time: endotracheal tubes, disposable ventilator circuits, cuff pressures monitors and closed multi-use catheter systems. The sponsor should also assist the researcher with training of the physicians and nursing staff in the management of products. Furthermore, the sponsor should assure the quality of the study. The sponsor should also assign

experts for the Expert Committee. In addition, the sponsor should provide funds for financial obligations of the research as listed in Table 1. 4.

1.18. TIME SCHEDULE

The preliminary timeframe of the research is listed in Table 1.3.

Table 1.3: Time schedule of the research

ACTIVITY	YEAR																
	2002			2003												2004	
	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB
Preparation of protocol																	
Permission from committees and institutions																	
Training of staff																	
Pilot study																	
Implementation and continuous training																	
Data collection																	
Data analysis																	
Report writing																	
Presentation of paper																	

1.19. FINANCIAL OBLIGATIONS

The sponsor has agreed to take responsibility for the financial obligations. Estimations were done as if all subjects were ventilated for 10 days and developed a ventilator-associated pneumonia as listed in Table 1.4.

Table 1.4: Financial obligations of the research

ITEMS	UNIT COST	QUANTITY	ESTIMATED COST
COST OF DATA COLLECTION AND END PRODUCT			
Photocopies of data collection forms			R 300.00
Language editing			R 2000.00
Printing and binding cost			R 2000.00
Writing of articles			R 2000.00
DIRECT COST OF SPONSOR			
Training at workshops			R 300.00
Cuff pressure monitoring devices	R 2 000.00	3	R 3 000.00
Disposable ventilator circuits	R 300.00	2x66	R 39 600.00
Closed multi-use catheter system	R 138.00	10x66	R 91 080.00
Hi-Contour™ endotracheal tubes	R 9.00	22	R 198.00
Hi-Lo™ Evac endotracheal tubes	R 140.00	22	R 3080.00
Hi-Lo™ Evac Lanz endotracheal tube	R 140.00	22	R 3080.00
Disposable rectal probes	R 40.00	66	R 2 640.00
Luki tubes	R 8.91	2x66	R 1176.12
Yankuer suction tips	R 8.50	2x66	R 1122.00
Bacterial filters	R 35.00	2x66	R 4 620.00
DIRECT EXPENSES OF RESEARCHER			
Telephone calls			R 100.00
Petrol			R 200.00
Rewards			R 300.00
TOTAL			**R 156 696.12**
AVERAGE PER PATIENT			R 2 374.18

1.20. CONCLUSIONS

This study will compare the effect of three types of endotracheal tubes on ventilator-associated pneumonia. The results will help the critical care nurse to implement measures to reduce morbidity, mortality and costs in the critical care setting. Chapter 2, 3, 4 and 5 is a review of literature regarding the definition, pathogenesis, diagnosis, risk factors, and preventative strategies of ventilator-associated pneumonia and prevention of silent aspiration.

CHAPTER 2
LITERATURE REVIEW
VENTILATOR-ASSOCIATED PNEUMONIA: DEFINITION, PATHOGENESIS AND DIAGNOSIS

2.1. INTRODUCTION

"The first requirement of a hospital is that it should do the sick no harm" was the comment of Florence Nightingale (Naikoba & Hayward, 2001:175).

Does the topic of ventilator-associated pneumonia pertain to the critical care nurse? The answer is emphatically "Yes". The critical care nurse is 24 hours a day responsible for the prevention, identification of symptoms and the management of the complications of ventilator-associated pneumonia. The critical care nurse, compared to the physician and the ancillary disciplines spends the most of the time at the bedside of the patient and cannot therefore turn a blind eye to the current views on ventilator-associated pneumonia.

The patient receiving mechanical ventilation has a 6 to 21 time higher risk of developing nosocomial pneumonia compared to the person who is not intubated (Mathews & Mathews, 2000:17). Pneumonia is the second most common nosocomial infection in the United States, and the leading cause of death as a result of nosocomial infection (Grap & Munro, 1997:419; Kollef, 1999:627). I believe that the South-African experience lines up with the same results, but no statistics on this matter are available. This emphasizes the need for developing statistics of the South African experience in different sites as well as to find solutions to this problem.

Ventilator-associated pneumonia is a nosocomial pneumonia that is not present at the time of intubation of the patient. It develops 48 hours or more after intubation when the patient is receiving mechanical ventilation (Grap & Munro, 1997:419). Some

writers differentiate between early-onset and late-onset ventilator-associated pneumonia. According to Smulders *et al.* (2002:858), early-onset ventilator-associated pneumonia is defined as pneumonia within 48-hours after intubation and late-onset pneumonia as pneumonia developing after 48-hours of intubation.

2.2. DIFFERENT DEFINITIONS OF VENTILATOR-ASSOCIATED PNEUMONIA

Some of the definitions of ventilator-associated pneumonia differ about the time of onset, but there is consensus about the content of definition.

Nosocomial pneumonia is pneumonia that develops after admission to a hospital. Ventilator-associated pneumonia is a nosocomial pneumonia that develops when a patient is receiving mechanical ventilation (Thompson, 1995:695) and that was not present at the time of intubation (Ellstrom, 1999:416).

“Ventilator-associated pneumonia is usually a bacterial nosocomial pneumonia that develops in patients with acute respiratory failure, supported by mechanical ventilation. This pneumonia was neither present nor incubated at the time of intubation” (Young & Ridley, 1999:1183).

Tasota, Fischer, Coulson and Hoffman (1998: Online) defines ventilator-associated pneumonia as: “as a nosocomial pneumonia that occurs more than 48 hours after hospital admission but is not incubated on admission, or is not known, because this type of pneumonia is not a reportable illness.” Grap and Munro (1997:419) and Mayhall (2001:200) also reiterate this definition.

The Centers for Disease Control and Prevention define ventilator-associated pneumonia as bacterial in origin, and have additional criteria of fever, leukocytosis, new and progressive lung infiltrates on chest radiography, purulent tracheobronchial

secretions and identification of a potential pathogen on gram stain smear (Thompson, 1995:695).

2.3. INCIDENCE, MORBIDITY, MORTALITY AND COST IN OTHER COUNTRIES

Ventilator-associated pneumonia is associated with increased mortality, morbidity and medical cost (Smulders, *et al*., 2002:858).

2.3.1. Incidence

Universally, the incidence of ventilator-associated pneumonia in mechanically ventilated patients is high. The incidence of this nosocomial pneumonia differs amongst researchers, because the diagnostic criteria for the diagnosis of nosocomial pneumonia differ. See Table 2.1 for a comparison of different references for incidence of ventilator-associated pneumonia.

Table 2.1: Comparison of incidence and mortality according to different references

INCIDENCE	MORTALITY	REFERENCE
10% to 65%	54% TO 71**%**	Grap and Munro (1997:419)
	13% to 55%	Thompson (1995:695)
	33% to 71%	Bowton (1999:28S)
1% per ventilator day		Grap and Munro (1997:419) Young and Ridley (1999:1183)
9% to 68%		Bowton (199:28S) Smulders *et al.* (2002:858)
Median of 4.7 to 34.4 per 1000 ventilator days		Thompson (1995:695)

The risk of developing ventilator-associated pneumonia increases with time and the patient is at the highest risk within the first two weeks of mechanical ventilation (Grap & Munro, 1997:419).

According to Grap and Munro (1997:419) the patient who receives mechanical ventilation has a 6 to 20 times higher risk of developing nosocomial infection 7 to 21 times higher risk, according to Young and Ridley (1999:1183).

The European Prevalence of Infection in Intensive Care (EPIC), identifies ventilator-associated pneumonia as the most common infection in European intensive care units amounting to 3 to 52% (Young & Ridley, 1999:1183).

2.3.2. Morbidity

Nosocomial pneumonia also contributes to an increase in morbidity of the patient. The development of a ventilator-associated pneumonia may increase hospital stay by an average of 7 to 9 days (Tasota *et al*., 1998: Online). Morbidity is associated with an increase in intensive care and hospital stay. Due to this prolonged stay, the patient is exposed to complications associated with invasive therapy and bed rest.

Morbidities associated with ventilator-associated pneumonia are increased bloodstream infections, 7 fold increase in days of mechanical ventilation, 2 to 5-fold increase in stay in intensive care unit, 2-fold increase in length of hospital stay. Nosocomial pneumonia also increases the incidence of septic shock (Harris & Miller, 2000:51).

2.3.3. Mortality

Ventilator-associated pneumonia is the leading cause of death of all nosocomial infections (Mathews & Mathews 2000:17).

For the mortality rates in different studies see Table 2.1. According to Young and Ridley (1999:1183), it is likely that many of the patients die with and not of ventilator-associated pneumonia. According to these writers, the mortality is 27% higher when *Pseudomonas aeruginosa* and *Acinetobacter* were cultured from endotracheal aspirates. The type of causative organism plays a bigger role in mortality.

2.3.4. Cost

The patient who survives an onslaught of ventilator-associated pneumonia will stay up to 5 to 7 days longer in the hospital (Grap & Munro, 1997:419; Shorr *&* O'Malley, 2001:228). This will therefore lead to an increase in medical cost, as only the stay in intensive care may be increased up to 9 days (Shorr *&* O'Malley, 2001:228).

In 1985 the annual spending for the treatment of nosocomial pneumonia in the United States was $1 billion. In 1991 the cost increased to between $5 billion and $10 billion although the prevalence remained the same (Tasota *et al.,* 1998: Online). According to Harris and Miller (2000:51), the direct annual cost related to the diagnosis and treatment of nosocomial pneumonia in the USA, is $2 billion. This is significant when considering that nosocomial pneumonia is preventable to some degree.

Financial concerns do not only apply to the private sector, but also to the public sector due to limited resources. For the patient this has financial implications due to higher to medical costs and loss of income.

2.4. PATHOGENESIS OF VENTILATOR-ASSOCIATED PNEUMONIA

The normal defenses and the pathogenic processes in the development of ventilator-associated pneumonia are discussed below.

2.4.1. Normal defenses against the development of pneumonia

The critical care nurse should understand the normal defenses against the development of pneumonia, to be able to take measures to prevent ventilator-associated pneumonia. The upper respiratory tract is the first line in the defense against invading organisms. The nose and oropharynx filter out the larger particles. Smaller particles deposit in the mucus membrane and are removed by cilia (Harris & Miller, 2000:53).

The lung's defense mechanisms against organisms reaching the lower respiratory tract, are the anatomy of the larynx and the presence of normal flora. If the bacteria bypass the upper airway defenses, and reach the lower airways, local and systemic cells will attempt to remove them. The local phagocytes and macrophage will attack the organisms. If this response is insufficient, the system macrophage accumulates at the site of the infection, due to the inflammatory response. Neutrophils and monocytes accumulate at this site to enable the phagocytes to remove the bacteria. If this process is unsuccessful, pneumonia develops (Harris & Miller, 2000:52, 53).

In the intubated patient the endotracheal tube bypasses the defenses of the upper airway. In the past, measures like closed suctioning procedures, the use of bacterial filters and meticulous hand washing were taken to prevent ventilator-associated pneumonia, do not prove to be effective.

2.4.2. Pathogenesis of the development of ventilator-associated pneumonia

In addition to understanding the normal defenses of the body against development of ventilator-associated pneumonia, the critical care nurse should understand the onslaught e.g. via intubation against these defenses. The process in the development of ventilator-associated pneumonia commences with colonization of the aerodigestive tract. These colonized endogenous organisms gain access to the lower respiratory tract via aspiration and translocation. Colonized exogenous organisms may also gain access to the lower respiratory tract, but this is not the main cause in the development of ventilator-associated pneumonia. Ventilator-associated pneumonia will develop if these organisms overcome the normal defenses of the body. The pathogenesis of ventilator-associated pneumonia is summarized in figure 2:1 and each of these aspects will be discussed in more detail.

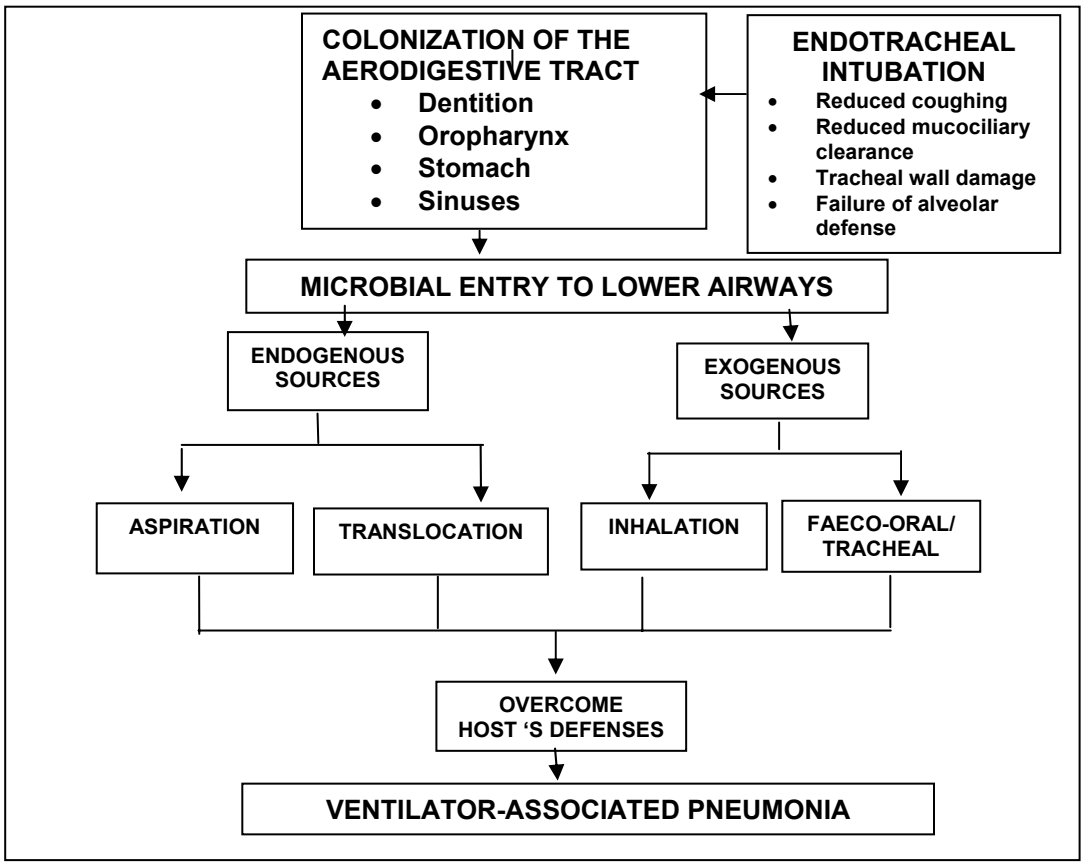

Figure 2.1: Pathogenesis of ventilator-associated pneumonia

2.4.2.1. Colonization of the aerodigestive tract

Colonization is the presence of an organism on the mucosa of the host, in the absence of any defense response. Pathogens or non-pathogens may be involved with colonization (Reese & Betts, 1996:946-947).

The pathogenesis of ventilator-associated pneumonia requires two important steps: colonization of the aerodigestive tract and the aspiration and/or inhalation of the contaminated secretions into the lower respiratory tract. Strategies to prevent ventilator-associated pneumonia should therefore include reduction of bacterial colonization in the aerodigestive tract and reduction of aspiration and/or inhalation, or both (Kollef, 1999:627).

Bacterial pathogen colonization of reservoirs like the oropharynx, sinuses, dentition and stomach take place in the patient who receives long-term mechanical ventilation.

Bacterial secretions from the oral, gastric and sinus cavities drain down into the oropharynx to the subglottic space (Young & Ridley, 1999:1183, 1187).

Sources of pathogens in colonization can either be exogenous, entering from the outside of body, or endogenous, in which case the patient is infecting himself (see Figure 2:1). In the past the cause of ventilator-associated pneumonia was attributed only to exogenous factors. The exogenous route of transmission is now better controlled with stringent infection control measures. The endogenous origin is presently considered to be the main cause of ventilator-associated pneumonia. "There is a direct relationship between upper gastrointestinal, oropharyngeal colonization and the occurrence of pneumonia" (Mahul, Auboyer, Jospe, Ros, Guerin, El Khouri, Galliez, Dumont & Gadin, 1992:20). Colonization occurs mostly in the dentition, oropharynx, stomach and sinuses. The "reservoirs" that can be colonized by organisms, including pathogens, will be discussed in more detail.

Dentition

Oral hygiene declines during the patient's stay in the intensive care unit and dental plaque can colonize with nonrespiratory pathogens like aerobic gram-negative bacteria and *Staphylococcus aureus.* As the patient's stay in the intensive care unit increases, the dental plaque increases. The dental bacterial flora frequently mirrors the bacteria in the endotracheal aspirates (Young & Ridley, 1999:1188). This indicates that dental plaque can be the origin of ventilator-associated pneumonia and emphasizes the importance of oral care in the intensive care unit.

Oropharynx

Nonpathogenic bacteria (gram-positive and anaerobic bacteria) predominantly colonize the oropharynx in normal circumstances. The lower respiratory tract is usually sterile. Normal flora occupy bacterial binding sites in the oropharynx to prevent colonization of gram-negative bacteria (Harris & Miller, 2000:53). However, this is not true about the hospitalized patient, in whom pathogens colonize. Pathogens usually include aerobic gram-negative bacteria (Lynch, 2001:376S; Young

& Ridley, 1999:1188). The use of antimicrobial therapy destroys the normal flora allowing pathogens to colonize at the binding sites and then to invade the oropharynx. In this stage the patient has no clinical evidence of infection (Harris & Miller, 2000:53).

In the case of other illness processes like sepsis, fibronectin decreases in the saliva. oropharyngeal inflammation and respiratory pathogens can release proteases that can degrade fibronectin. The role of fibronectin is to coat the oropharynx and is secreted together with saliva. Fibronectin favours the binding of commensal oral streptococci and coats the buccal epithelium. Reduced fibronectin leads to abnormal colonization of the oropharynx with aerobic gram-negative organisms (Tablan, Anderson, Besser, Bridges & Hajjehal, 2003: Online; Young & Ridley, 1999:1188). Table 2.2 lists common these organisms including gram-negative bacteria.

Colonization of the oropharyngeal secretions is one of the major causes of nosocomial pneumonia. There is a correspondence between the organisms cultured in the oropharynx and those that caused ventilator-associated pneumonia (Grap & Munro, 1997:420; Harris & Miller, 2000:56). The general perception is that these colonized secretions accumulate on top of the endotracheal tube cuff, leak past the cuff and cause colonization of the lower respiratory tract.

Secretions that accumulate on top of the cuff can also leak into the lower respiratory airways, when the patient self-extubates, or when the cuff is deflated for the repositioning of endotracheal tubes. The bolus of secretions provides a large inoculum to the lower respiratory tract and therefore increases the risk of ventilator-associated pneumonia (Harris & Miller, 2000:56). This may also be true when patients are extubated or when their position is changed without subglottic suctioning.

Stomach

The stomach is usually sterile because of the presence of hydrochloric acids. Colonization of the stomach takes place if there is a change in the pH (Harris & Miller, 2000:54). The stomach can serve as a reservoir for aerobic gram-negative bacteria.

The use of H_2 -antagonists and antacids increase the pH of the stomach leading to an increased rate of gastric colonization. This is however not the case with sucralfate (Young & Ridley, 1999:1188). Gastric and duodenal enteral feeding further increases the risk for colonization. According to Young and Ridley (1999:1189), studies have not consistently shown that gastric colonization is the preceding site of colonization in ventilator-associated pneumonia. However, many gastrointestinal organisms were found to be the cause of ventilator-associated pneumonia. Therefore, selective decontamination of the digestive tract is practice in many centers (Young & Ridley, 1999:1189).

The use of selective decontamination of the digestive tract, H_2 -antagonists and antacids are usually not a practice at the study site. Sucralfate is prescribed as preventative management for gastric ulcers of the ventilated patient.

Sinuses

Nasotracheal and nasogastric tubes may lead to nosocomial sinusitis. Clinical signs are not obvious and areusually under-diagnosed. There is a relationship between sinusitis and ventilator-associated pneumonia. The organisms cultured from the sinuses are predominantly gram-negative bacteria (Young & Ridley, 1999:1188). In one study the same organism was cultured from the sinuses and a bronchial lavage in 38% of ventilated patients. The presence of nasogastric tubes and/or nasotracheal tubes were associated with the development of maxillary sinusitis (Thomson, 1995:699). The issue of oral versus nasal intubation is still unresolved, but oral intubation was utilized in the majority of subjects of this study. The Centers for Disease Control and Prevention recommend the removal of tubes as soon as they are not necessary, as a preventative measure against ventilator-associated pneumonia (Thomson, 1995:699).

2.4.2.2. Effects of intubation on the host's defense mechanisms against colonization

The host has various defense mechanisms against colonization e.g. coughing mucociliary clearance, tracheal wall and alveolar defenses. When a patient is intubated, these defense mechanisms are affected. The effect of the endotracheal tube will be discussed according to each defense mechanism.

Coughing

In normal circumstances, pulmonary secretions and microorganisms are mechanically coughed out. In case of intubation, the endotracheal tube bypasses the epiglottis and coughing is not so effective as in normal circumstances. The endotracheal tubes interfere with the coughing process (Kollef, 1999:627). Factors like the use of sedatives, opioid, analgesia, neuromuscular blocking agents (Young & Ridley, 1999:1190) and suppression of level of consciousness (Harris & Miller, 2000:55) will attribute to suppression of the cough reflex.

The presence of medical devices contributes to the pathogenesis of ventilator-associated pneumonia. Nasogastric tubes contribute to gastric reflux and increase the potential for aspiration. Endotracheal tubes can contribute to the pathogeneses by facilitating bacterial colonization of the tracheobronchial tree with colonized secretions that accumulate on top of the cuff. These secretions are aspirated into the lower respiratory airways. The presence of these devices obviously makes effective coughing and swallowing difficult for the patient.

Mucociliary clearance

The function of cilia in the trachea can be compared with a broom dusting the floor. It propels viscous mucus and debris towards the larynx for expectoration (Young & Ridley, 1999:1190). Firstly, the endotracheal tube is a physical barrier to cilial function. Secondly, the endotracheal tube reduces tracheal mucus velocity (Young & Ridley, 1999:1190).

Increased oxygen concentration, according to Young and Ridley (1999:1190), may lead to tracheobronchial inflammation, epithelial sloughing and a progressive reduction in tracheal mucus velocity.

Adequate warming and humidification of the inspired oxygen is essential in the maintenance of the cilia and the liquefying of secretions. Inadequate humidification leads to damage and dehydration of the cilia. Therefore, impairment of the mucociliary elevator will follow. The duration of ventilation with dry gases will determine the degree of damage to the cilia (Young & Ridley, 1999:1190). This will therefore predispose the patient for the development of ventilator-associated pneumonia.

Tracheal wall defenses

Medical devices like the cuff and the tip of the endotracheal tube can cause mechanical damage to the tracheal wall. Suction catheters and movement of the endotracheal tube can also cause further damage to the tracheal wall, resulting in bacterial adhesion. Damage to the tracheal wall impairs the function of neutrophils and macrophages in the mucus membrane responsible for defenses against bacterial invasion (Young & Ridley, 1999:1190).

Aspiration may cause chemical damage to the tracheal wall. “Bile and gastric aspiration may exacerbate the injury and delay healing” (Young & Ridley, 1999:1190). Micro- or macro-aspiration of these substances take place.

Alveolar defenses

Alveolar defenses depend upon the release of opsonins in the fluid lining of the epithelium. The opsonin interaction enhances macrophage and phagocyte release. The alveolar macrophages release neutrophils. When the neutrophils bind to the invader, it facilitates their migration into the interstitium and ultimately to the alveoli. The effectiveness of the defense mechanisms will depend on the size of the

inoculum. Even the healthy person's defenses will be overwhelmed if the alveoli are exposed to an excessive bacterial load (Young & Ridley, 1999:1190).

During the suctioning procedure the alveoli are directly exposed to bacteria. When a suction catheter is passed down the endotracheal tube, up to 60 000 viable colonies of bacteria can be dislodged. The installation of only 5ml of normal saline into the endotracheal tube can mobilize 310 000 colonies of bacteria (Tasota *et al.,* 1998: Online).

2.4.2.3. Mechanisms of microbial entry

In fact, the intubated patient is protected against airborne bacteria (exogenous source), but another route for non-airborne pathogens in particular; the artificial airway (endogenous source) that bypasses the normal defense mechanisms, are introduced (Mathews & Mathews 2000:17).

Endogenous sources

The following two mechanisms are associated with **endogenous sources** of colonization (see Figure 2.1).

a) Aspiration past the endotracheal tube cuff

The critically ill, ventilated patient is in general positioned supine. Oropharyngeal secretions pool in the subglottic space above the cuff of the endotracheal tube, forming a reservoir for these colonized secretions (Young & Ridley, 1999:1188) (see Figure 1.2). Stasis of contaminated mucous and secretions take place between the superior edge and the glottis, called the subglottic space. The inflation of the cuff does not totally prevent these secretions for leaking past the cuff (Mahul *et al*., 1992:20; Shorr & O'Malley, 2001:229). Leakage past the cuff is considered to be the main cause of ventilator-associated pneumonia (Young & Ridley, 1999:1183). Coughing and slight movement of the endotracheal tube causes these secretions to leak past the cuff (Thomson, 1995:698). In 66% of cases, the organism that caused

pneumonia was the same organism that colonized in the oropharynx (Harris & Miller, 2000:54).

b) Translocation

Translocation is when bacteria or bacterial products cross from the intestine to either vasculature or mesenteric lymph nodes. Organisms can be transmitted to the lungs, the thoracic cavity, blood and the lymph system (Thompson, 1995:696). The organisms can, if not overcome by the defense mechanisms or antimicrobial therapy, proliferate and spread to the efferent lymphatic system and portal system (this however, has not been extensively researched in humans) (Harris & Miller, 2000:52; Thompson, 1995:698).

In the ventilated patient, organisms may translocate from the subgingival plaque, peridontal areas, oropharynx, sinuses, stomach and trachea. Translocation is an important step in the development of ventilator-associated pneumonia (Young & Ridley, 1999:1187). Antibiotic therapy is not recommended for this particular phenomenon, as it resulted in opportunistic infections and diarrhea. It is well-accepted practice in the prevention of translocation of bacteria, to commence enteral or parental nutrition as soon as possible (Thompson, 1995:699).

Exogenous sources

The following two mechanisms are associated with **exogenous sources** of colonization.

a) Inhalation of contaminated aerosols

The following mechanism is associated with intubation and mechanical ventilation. Contamination of respiratory equipment and devices plays a major role in this case. Treatment-related and infection control-related risk factors will be discussed in Chapter 3.

b) Faeco-oral or faeco-tracheal route

Nursing or medical staff can play a role in cross-colonization or transfer of rectal bacteria. This can be prevented by adherence to infection control measures (Young & Ridley, 1999:1189). This route should not play a major role in the pathogenesis of ventilator-associated pneumonia, as it could be prevented.

2.4.2.4. Overcoming of the hosts defenses

The risk of developing ventilator-associated pneumonia will also depend on the microbial load delivered as well as the virulence of the organism. Healthy people rarely have gram-negative bacteria in the oropharynx, but within a few days after admission to a hospital, the critically ill will be colonized with gram-negative bacteria (Thompson, 1995:696).

Secretions from the oropharynx that leak past the cuff of the endotracheal tube find a way to the lower respiratory tract. The presence of the endotracheal tube contributes to the process of colonization (Smulders *et al*., 2002:858). Bacteria can multiply if the host's defense mechanism is overwhelmed. This leads to an inflammatory response in the alveoli, causing "congestion, leukocyte and macrophage infiltration and fibrinuous exudation into the alveoli" (Young & Ridley, 1999:1183). This inflammatory response occurs more than 48 hours after intubation and is called ventilator-associated pneumonia (Young & Ridley, 1999:1183).

Colonized organisms then multiply in the lower respiratory tract. This will trigger neurtophils to accumulate in peripheral bronchi and alveolar spaces. The development of a ventilator-associated pneumonia will depend on the bacterial load aspirated as well as mechanical, humoral and cellular defenses of the lungs. Phagocytes are mobilized in response to the inflammatory response (Harris & Miller, 2000:52).

Due to changes in the surface of the epithelial cells, pH and mucin in the lung secretions, organisms adhere increasingly in the critically ill patient. If the bacterial

load is great enough, the inflammatory response will extend to the bronchial wall (causing bronchiolitis) then to the alveolar septa (leading to bronchopneumonia) and surrounding areas (Thompson, 1995:696).

2.5. DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA

The following will be discussed in more detail: classification of organisms contributing to and the diagnosis of ventilator-associated pneumonia.

2.5.1. Classification

Ventilator-associated pneumonia is divided into early-onset and late-onset ventilator-associated pneumonia. Most cases of ventilator-associated pneumonia develop within the first 3 to 10 days of intensive care stay and few develop between 16 to 21 days. Nosocomial pneumonias are classified according to the time of onset and the type of organism involved (Harris & Miller, 2000:56). Some writers do not distinguish between early-onset and late-onset ventilator-associated pneumonia and define ventilator-associated pneumonia only as nosocomial pneumonia that develops after 48 to 72 hours (Kollef, 1999:627).

2.5.1.1. Early-onset ventilator-associated pneumonia

Smulders *et al.* (2002:858) define early-onset ventilator-associated pneumonia as pneumonia that develops within 48 hours of intubation. Early-onset ventilator-associated pneumonia is usually caused by community-acquired pathogens and is rarely multi-resistant to antimicrobial therapy (Lynch, 2001:374S). In a study where early-onset ventilator-associated pneumonia was defined as pneumonia in the first 4 days of intubation, the ventilator-associated pneumonia was associated with organisms from the oropharyngeal bacterial species like *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Staphylococcus aureus* (Grap & Munro, 1997:422). Young and Ridley (1999:1193) additionally mentioned *Enterobacteriaceae* species. Harris and Miller (2000:56) also mentioned *Proteus*, *Serratia*, *Klebsiella* and *Escherichia coli*.

2.5.1.2. Late-onset ventilator-associated pneumonia

Late-onset ventilator-associated pneumonia is considered as a hospital acquired pneumonia. Late-onset ventilator-associated pneumonia is associated with gram-negative organisms that also have their origin in the gastrointestinal tract. Examples of this type of organism, according to Young and Ridley (1999:1193), are *Pseudomonas aeruginosa, Acinetobacter* species and methicillin-resistant *Staphylococcus aureus*.

2.5.2. Contributing organisms

The following is not a complete discussion of all organisms involved in ventilator-associated pneumonia, but a highlight of some of the characteristics of these organisms. See Table 2.2 for a list of microorganisms often associated with ventilator-associated pneumonia.

Frequently cultured gram-negative organisms are *Pseudomonas aeruginosa, Acinetobacter species, Proteus species, Haemophilus species, Branhamella catarrhalis, Klebsiella species and Enterobacter cloacae.* The frequently found gram-positive organisms are *Staphylococcus aureus, Streptococcus pneumoniae*, other streptococci and Corynebacterium species (Young & Ridley, 1999:1184). Polymicrobial gram-negative organisms frequently cause ventilator-associated pneumonia (Thompson, 1995:696).

Pseudomonas aeruginosa and *Acinetobacter baumannii* or *calcoaceticus* are the causative organisms in ventilator-associated pneumonia in mechanically ventilated patients in 30 to 50% of hospital-acquired pneumonias. These organisms usually display multiple-resistance against antibiotic drugs (Harris & Miller, 2000:56).
One study has implicated *Pseudomonas aeruginosa*, Acinetobacter or *Xanthomonas maltophilia* as “high-risk” pathogens, as they attributed to 65% of the mortality rate compared to the mortality rate in early onset pathogens that is 31% (Lynch, 2001:373S and 374S).

Pseudomonas aeruginosa has been implicated in colonization of the oropharynx or trachea in the critically ill patient with prolonged hospital stay and severe illness. Factors that also played a role were hospitalization longer than 10 days, prior use of third-generation cephalosporins, surgical emergencies and alcoholism (Lynch, 2001:376S).

However, *Pseudomonas aeruginosa* may colonize the trachea without colonization of the oropharynx (Young & Ridley, 1999:1180). *Pseudomonas aeruginosa is* associated with a high mortality rate and specific preventative measures should be the focus for this organism (Rello, Rué, Jubert, Muses, Sonora, Vallés & Niederman, 1997:1862,1867).

Acinetobacter is associated with a high mortality rate and with resistance against multiple antibiotics. The hands of health care providers, contaminated nebulizers, reservoirs and fiberoptic bronchoscopes are often mentioned as causes of transmission of Acinetobacter (Baraibar, Correa, Mariscal, Gallego, Vallés, & Rello, 1997:1050). Comorbid illness, severity at hospital admission, or exposure to antibiotic therapy could not be related to the organism. The culprit identified was cross-contamination during the manipulation of the airway (Baraibar *et al.,* 1997: 1054).

Prior antibiotic use, especially broad-spectrum antibiotics, leads to colonization or infection with *Pseudomonas aeruginosa*, *Acinetobacter*, methicillin-resistant *Staphylococcus aureus* and other antibiotic-resistant bacteria (Lynch, 2001:374S). Antibiotic resistance has increased over the last 20 years worldwide. The prevalence of some pathogens like *Acinetobacter* and methicillin-resistant *Staphylococcus aureus,* has increased; whereas organisms like *Klebsiella pneumonia* and *Pseudomonas aeruginosa* remained stable or declined (Lynch, 2001:374S).

The American Thoracic Society identified the following core organisms*:* Enterobacter sp*., Escherichia coli,* Klebsiella sp*.,* Proteus sp*., Serratia marcescens, Hemophilus*

influenzae, gram-positive organisms like methicillin-sensitive Staphylococcus aureus and Streptococcus pneumoniae. In the absence of risk factors, patients with mild-to moderate nosocomial pneumonia are usually infected with abovementioned core organisms (American Thoracic Society, 1996:1713).

Identification of the causative organism is often difficult, but some will be of assistance. The severity of the illness, duration of hospital stay, and prior antibiotic exposure will give clues to the causative organism (Lynch, 2001:373S). The type of organism involved indicates the route of transmission. Aspiration of oropharyngeal colonizers is the most frequent, but organisms like *Legionella* and *Hemophilus influenzae* are delivered by droplet or aerosol route (Thompson, 1995:696).

Anaerobic bacteria are not often mentioned as causative organisms in nosocomial pneumonia, but Craven and Steger (1995:3S) list the following: *Peptostreptococcus,* Fusobacterium sp., Peptococcus sp., *Bacteroides melaninogenicus and Bacteroides fragilis.*

Bacteria are not the only organisms that can cause ventilator-associated pneumonia, but also fungi and viruses (Thompson, 1995:695). Literature often refers to bacterial pneumonia, but fungal and viral infections are often omitted. This may be that the diagnosis has to be made by the use of bronchoscopy (Craven & Steger, 1995:11S).

About 75% of fungal infections in the USA were nosocomial infections and 44% included intensive care patients (Eggimann & Pittet, 2001:2067). Aspergillus pneumonia is uncommon, but is associated with a high mortality and is often found in patients with a compromised immune system, like AIDS and those undergoing chemotherapy or organ transplant (Craven & Steger, 1995:11S).

The most common respiratory viruses causing nosocomial pneumonia are influenza and respiratory syncytial virus. Most nosocomial outbreaks are associated with community outbreaks. Influenza pneumonia is seen in intensive care units and in

pediatric wards and chronic facilities. Spreading of the organism is by person-to-person contact via large droplets, close contact, but transmission can also by hand or fomites (Craven & Steger, 1995:10S).

Respiratory syncytial virus is common during infancy and childhood and is usually mild, except in the immune compromised child or in those having chronic cardiac or pulmonary disease. Transmission is also via close contact or contamination of hands and fomites (Craven & Steger, 1995:10S).

Table 2.2: Microorganisms cultured from respiratory tract obtained from adults (Craven & Steger, 1995:3S; Tablan, *et al*., 2003: Online)

BACTERIA
Aerobic bacteria
Gram-negative bacilli *P aeruginosa* Enterobacter sp Klebsiella sp *E coli* Serratia sp Proteus sp Citrobacter sp *Acinetobacter alcoaceticus/ baumanii* *H influenzae* Legionella sp *B catarrhalis* Corynebacterium sp *X maltophilia*
Gram-positive cocci *S aureus* Streptococcus sp Corynebacterium sp.
Anaerobic bacteria
Peptostreptococcus Fusobacterium sp Peptococcus sp *Bacteroides melaninogenicus* *B fragilis*
FUNGI
Aspergillus sp Candida sp

VIRUSES
Adenovirus Influenza virus Parainfluenza virus Respiratory syncytial virus (RSV)

2.5.3. Diagnostic criteria

The diagnosis of ventilator-associated pneumonia differs from institution to institution and is quite controversial. The golden standard has not yet been reached. The ideal will be to base the diagnosis on histological and bacteriological findings (Grap & Munro, 1997:422), but this is not practical and can only be obtained through open lung biopsy. Although very accurate it is not practical.

We are therefore left with details like clinical picture, physical assessment and radiological findings to determine the presence of a ventilator-associated pneumonia. Attempts were made to define the presence of nosocomial pneumonia. See the Center for Disease Control and Prevention's criteria in Table 2:3. Criticism against these criteria is that it is subjective. Pulmonary infiltrate and fever may also be caused by aspiration, atelectasis, pulmonary embolism, pulmonary edema, adult respiratory distress syndrome, pulmonary hemorrhage, lung contusion, tumor, radiation pneumonitis and drug reaction (Grap & Munro, 1997:422). Thompson (1995:695) named some more noninfectious causes of lung infiltrations: congestive heart failure, tumors, pulmonary emboli and fibrinoproliferation of acute respiratory distress syndrome.

The golden standard for the diagnosis of ventilator-associated pneumonia, according to Young and Ridley (1999:1184), is to combine histopatological and microbiological examination for the presence of the inflammatory response as well as the presence of the microorganism. It may be impractical to obtain a histological sample from a critically ill patient due to the complications involved. Clinical diagnosis specifically,

rales and dull percussion are non-specific in the patient that is receiving mechanical ventilation.

Only three of the criteria for the diagnoses of ventilator-associated pneumonia will be listed, but there are many other criteria available. The Centers for Disease Control and Prevention propose the criteria for the diagnosis of nosocomial pneumonia (Table 2:3) and the American Thoracic Society (Table 2:4) considers the patient who is already in an intensive care unit, or receiving mechanical ventilation. The modified version in Table 2.5 is the third criteria and was used in this research, as it was more practical for the diagnosis of ventilator-associated pneumonia selected by the blind investigator.

TABLE 2.3: Centers for disease control and prevention's criteria for nosocomial pneumonia

Pneumonia must meet at least one of the following criteria:

Criterion 1:

Patient has rales or dullness to percussion on physical examination of the chest.

And at least one of the following:

a. New onset of purulent sputum or change in character of the sputum
b. Organisms cultured from the blood
c. Isolation of an etiologic agent from the specimen obtained by transtracheal aspirate, bronchial brush or biopsy

Criterion 2:

Patient has a chest radiographic examination that shows new or progressive infiltrate, consolidation, cavitation or pleural effusion

And at least one of the following:

a. New onset of purulent sputum or change in character of the sputum
b. Organisms cultured from the blood
c. Isolation of an etiologic agent from the specimen obtained by transtracheal aspirate, bronchial brush or biopsy
d. Isolation of virus from or detection of viral antigen in respiratory secretions
e. Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for pathogen
f. Histological evidence of pneumonia

(Grap & Munro, 1997:423).

Table 2.4: American Thoracic Society's definition of severe hospital- acquired pneumonia

ADMISSION CRITERIA TO THE INTENSIVE CARE UNIT
❑ Respiratory failure, defined as the need for mechanical ventilation or the need for > 35% oxygen to maintain an arterial oxygen saturation > 90%
❑ Rapid radiographic progression, multilobar pneumonia, or cavitation of a lung infiltrate
❑ Evidence of sever sepsis with hypotension and/or end-organ dysfunction:
➢ Shock (systolic blood pressure < 90mmHg or diastolic blood pressure < 60mmHg)
➢ Requirement for vasopressor for more than 4 hr
➢ Urine output < 20ml/hr or total urine output < 80ml in 4hr (unless another explanation is available)
➢ Acute renal failure requiring dialysis

(Grap & Munro, 1997:423)

Table 2.5: Modified criteria for the diagnosis of ventilator-associated pneumonia

Young and Ridley (1999:1184) has adapted the diagnostic criteria to the following:
a. Fever of > 38.3° C, leucocytosis and deterioration of gas exchange,
b. Radiographic appearance of new and persistent infiltrates
c. Grossly purulent tracheobronchial secretions.

Some more different criteria exist to define pneumonia (Cook *et al*., 1998:782-784) as indicated in Table 2.3, 2.4 and 2.5. These tables list the definition of the definitions of the Centers for Disease Control and Prevention, the American Thoracic Society and modified criteria as by Young and Ridley. These criteria will not be discussed, but it just indicates that there is no gold standard for the diagnosis of pneumonia and therefore ventilator-associated pneumonia. Those listed here are the generally accepted criteria.

2.5.3.2. Sampling of pulmonary specimens

Sampling pulmonary secretions for microscopic culture and sensitivity are not cut-and-dry. There are different methods of obtaining sampling pulmonary secretions and no ideal method exists (Grap & Munro, 1997:423), as tracheobronchial colonization is normal in mechanically ventilated patients. To differentiate between

colonization and infection is complicated. To exclude tracheobronchial contamination, protected specimen brush and bronchoalveolar lavage is suggested (Grap & Munro, 1997:423).

Protected specimen

Protective brush biopsy is obtained when a sample brush covered with a sterile cannula is introduced with a flexible bronchoscope to the affected area. A small tissue sample is then obtained. Due to the size of the sample the sensitivity is reduced (Grap & Munro, 1997:424).

Bronchoalveolar lavage

Bronchoalveolar lavage is where 120ml sterile saline is injected into the affected lung tissue and the fluid is aspirated again (Grap & Munro, 1997:424). The sample can be examined with a microscope and a culture and sensitivity can also be obtained.

Neither of there two methods has been proven to be superior (Grap & Munro, 1997:424). The protected specimen brushing cultures had a mean sensitivity of 82% and a mean specificity of 92% and bronchio-alveolar lavage had a mean sensitivity of 86% and a mean specificity of 87% (Young & Ridley, 1999:1186).

Both these procedures are not without problems and complications, as they are invasive procedures. The cost factor must also be considered. Other complications include cardiac arrhythmias, hypoxemia, bronchospasms, bleeding and pneumothorax (Grap & Munro, 1997:424).

Transthoracic needle biopsy

Transthoracic needle biopsy has a low sensitivity and is attributed to the small size of the sample. The risk for developing a tension pneumothorax is high, if the patient is receiving mechanical ventilation (Grap & Munro, 1997:422).

Endotracheal aspirate sampling

A widespread method of obtaining a pulmonary specimen is with endotracheal aspiration. A sterile suction catheter is introduced down the endotracheal tube into the proximal bronchial tree or trachea. Suctioning is applied and the suction catheter is withdrawn. The origin of the bacteria may be from either the bronchus or the trachea and may be contaminated by organisms from the endotracheal tube itself (Young & Ridley, 1999:1187). The mean sensitivity with this technique is between 44% and 100% and the mean specificity is between 52% and 100% (Grap & Munro, 1997:424) and according to Young and Ridley (1999:1186) the mean sensitivity is 78% (69% in another study) and the mean specificity is 19% (80% in another study).

This method has been chosen for this research due to the cost and complications involved with the other techniques. The endotracheal aspirate allows for earlier identification of the organisms, as the other methods are more labour intensive. The endotracheal aspirate sampling is a simple procedure and can even be performed by nursing staff.

Smulders *et al.* (2002:856) made use of the tracheobronchial sample with a sterile catheter in their study. The samples were taken twice a week, as is the case in this study.

Analysis of pulmonary secretions

The analysis of microscopic cultures is important because it does not only identify the pathogen, but also give clues of the mechanism of infection. If organisms from the gastrointestinal tract or oropharyngeal tract are cultured, the origin is self-contamination. If the organism has it's origin in the environment, the organism cultured will be an environmental pathogen (Grap & Munro, 1997:425).

Ventilator-associated pneumonia is usually caused by more than one pathogen. This makes the interpretation of specimen samples more complicated (Grap & Munro, 1997:425). The diagnosis of a ventilator-associated pneumonia is not only made on

the positive culture of a pathogen, but it confirms the diagnosis made on the clinical presentation of the patient. It therefore directs the type of treatment, but is not an absolute requirement for antimicrobial therapy.

2.5.3.3. Blood cultures

In a study where bronchoalveolar lavage and blood cultures were compared, the conclusion was that blood culture does not detect the same organism as the bronchoalveolar lavage. It did not predict complications, length of stay in intensive care unit, and severity of illness. The only purpose for blood cultures in the patient with ventilator-associated pneumonia, is to confirm a suspicion of another probable infectious condition (Luna, Videla, Mattera, Vay, Famiglietti, Vujacich, & Niederman, 1999:1075).

2.5.3.4. Analyses of chest radiography

New progressive pulmonary infiltrates may indicate the presence of ventilator-associated pneumonia. To identify a new or progressive pulmonary infiltrate is sometimes difficult as the bedside films are often of poor quality. Noninfectious causes also attribute to infiltrates in the critical ill patients (Grap & Munro, 1997:423; Thompson, 1995:695). According to Young and Ridley (1999:1185), only 44% of pulmonary densities on intensive care unit chest radiographs are of an infectious origin. Pulmonary hemorrhage, chemical aspiration, pleural effusion, congestive heart failure, acute respiratory failure, tumor, atelectasis and pulmonary embolism may cause pulmonary infiltrates (Mayhall, 2001:200).

According to the blind investigator, lung conditions like lung carcinoma and metastasis, cystic fibrosis and tuberculosis can make the interpretation of chest radiographic investigations difficult and was listed under screening criteria.

2.5.3.4. Pyrexia

Ventilator-associated pneumonia is associated with the development of pyrexia. However, other causes of pyrexia could be other infections like urinary tract infection,

intra-abdominal infections and bacteremia (Meduri, Mauladin, Wundrink, Leeper, Jones, Tolley & Marshall, 1994:221). Drug reaction, extrapulmonary infection, blood transfusion and extrapulmonary inflammation may also cause fever, in the mechanically ventilated patient (Mayhall, 2001:200).

2.5.3.5. Leukocytosis

Leukocytes (also called white blood cells) are the main players in both the inflammation and immune response of the body. Lymphocytes are one type of leukocytes responsible for governing immunity and antibody production (Borton, 1996:26).

Elevated leukocyte count does not provide a clear-cut diagnosis of the presence of an infection. Conditions that may reduce the leukocyte count are trauma and steroid therapy (Borton, 1996:28). Both these factors influence the subject enrolled in the research, surgery and steroid therapy.

2.5.3.6. Appearance of pulmonary secretions

Purulent secretions have been used as a criterion for the presence of ventilator-associated pneumonia (Mayhall, 2001:200). A change in colour and volume may be an important clue of the presence of pneumonia.

On its own, not one of the above-mentioned criteria indicates the presence of ventilator-associated pneumonia and all the criteria for the diagnosis of ventilator-associated pneumonia should be considered.

2.6. CONCLUSION

One of the most severe complications of mechanical ventilation is ventilator-associated pneumonia. Ventilator-associated pneumonia is associated with a high mortality, morbidity and cost. The pathogenesis depends on colonization of the aerodigestive tract and pooling of secretions on top of the cuff in the subglottic space. These secretions leak past the cuff into the lower respiratory tract.

The diagnosis of ventilator-associated pneumonia will always be a contentious subject as it a clinical diagnosis. The diagnosis should be done in the light of the patient's medical history, clinical, laboratory and radiographic data.

The critical care nurse should be proficient in the identification of the clinical signs and symptoms of ventilator-associated pneumonia and the analysis of laboratory and radiographic data, as this will make the collection of the information more meaningful. The critical care nurse can play a more active role in the identification of risk factors, diagnosis and prevention measures in ventilator-associated pneumonia.

CHAPTER 3
LITERATURE REVIEW
RISK FACTORS IN THE DEVELOPMENT OF VENTILATOR-ASSOCIATED PNEUMONIA

3.1. INTRODUCTION

Insight into the risk factors associated with the development of ventilator-associated pneumonia will enable the critical care nurse to understand the importance of limiting these risk factors in the prevention of ventilator-associated pneumonia.

Risk factors may present themselves in combinations in the same patient and increases the likelihood of developing pneumonia even more. Risk factors are divided into three groups namely: host-related, treatment-related and infection-control related risk factors (Harris & Miller, 2000:55). See Figure 3.1.

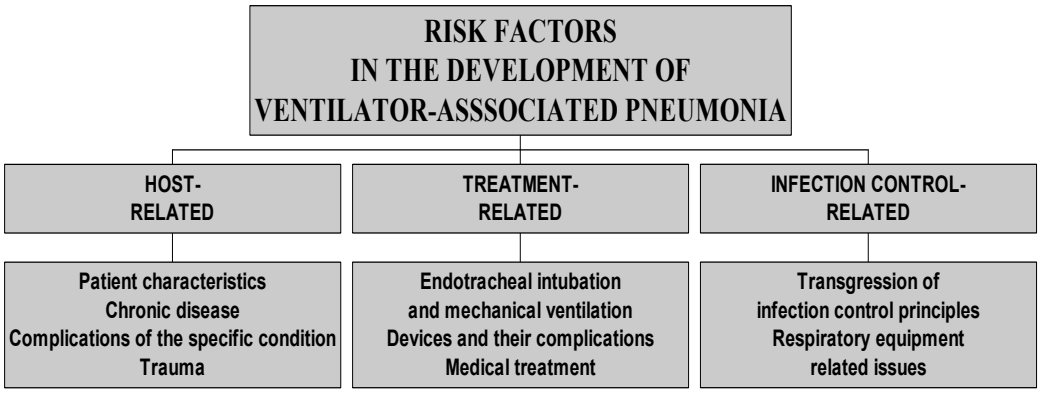

Figure 3.1: Risk factors in the development of ventilator associated pneumonia

Risk factors in the development of ventilator-associated pneumonia are highlighted in Table 3.1. The discussion on risk factors is not comprehensive, but only explains the aspect that needs clarification, as some of the risk factors are apparent. Many of these risk factors are interlinked and can occur in combinations.

Table: 3.1: Risk factors associated with ventilator-associated pneumonia and references.

RISK FACTORS	REFERENCES
HOST-RELATED	
Patient characteristics	
❑ Age (greater than 65 to 70)	1,3,5,6
❑ Smoking	1.5
❑ Dental plaque	1
Chronic diseases	
❑ Chronic obstructive pulmonary disease	1,5,6
❑ Cardiopulmonary, renal liver, and neurological disease and diabetes mellitus	1,3,5
❑ Compromised immune system	2
❑ Alcoholism	3,5
Complications of the specific condition:	
❑ Acidosis	1
❑ Altered level of consciousness	1,3
❑ Severity of illness	1,3,5
❑ Physical and psychological response to stress	3
❑ Malnutrition	1,3,5
❑ Shock	1,6
❑ Sleep deprivation	3
Trauma	
❑ Burn trauma	1
❑ Severe head trauma	1,5
❑ Chest trauma	1,5
TREATMENT-RELATED	
Endotracheal intubation and mechanical ventilation	
❑ Endotracheal intubation	2,3,4,5
❑ Mechanical ventilation	1,2,3
❑ Re-intubation or self-extubation	1,4
Devices and their complications	
❑ Nasogastric tube	1,2,4,5
❑ Enteral feeding increases gastric pH	1,2,5
❑ Aspiration, micro-emesis and micro-aspiration	2,5
❑ Presence of intracranial pressure monitor	1
❑ Bronchoscopy	1, 5
Medical treatment	
❑ Indiscriminate use of antibiotic therapy	1,4,5
❑ Broad-spectrum antibiotic therapy	2,3
❑ Elevated gastric pH	1,2
❑ Histamine$_2$–receptor antagonists	1,3,4,5
❑ Selective gastric decontamination	4
❑ Head surgery	1

RISK FACTORS	REFERENCES
❑ Upper abdominal or thoracic surgery	1,3,5
❑ Supine position	1,3,4,5
❑ Immunosuppressive agents	3,6
❑ Inadequate pain control	5
INFECTION CONTROL-RELATED	
Transgression of infection control principles	
❑ Poor hand washing techniques and non-adherence to universal precautions	1,2,4,5
❑ Poor suctioning techniques by care givers	2
❑ Understaffing	3
Respiratory equipment-related issues	
❑ Respiratory equipment contamination and spillage	2,4,5
❑ Changing of ventilator tubing more often than every 48 hours	1,4,5

Keys to references in Table 3.1

1) Harris & Miller, 2000:54-56
2) Mathews & Mathews, 2000:18
3) Tasota *et al*. 1998: Online
4) Grap & Munro, 1997:420-422
5) Ellstrom, 1999:418-419
6) Lynch 2001:375S

3.2. HOST-RELATED RISK FACTORS

Host-related factors are those characteristics related to the person which increases the risk for the development of ventilator-associated pneumonia. Host-related factors increase colonization in the oropharynx and in the stomach. Some of the risk factors can also contribute to the development of ventilator-associated pneumonia, by allowing bacteria to enter the lungs or to impair lung defenses against bacteria (Harris & Miller, 2000:55). Host related factors refer to patient characteristics, chronic diseases, complications of specific conditions and trauma.

3.2.1. Patient characteristics

The risk factors age, smoking and dental plaque related to patient characteristics are discussed below.

3.2.1.1. Age

The elderly (older than 65 years) are more susceptible to infection than younger patients (48% of patients admitted to intensive care units are older than 65 years.) Mortality due to nosocomial pneumonia is 5 times higher in the elderly. This is ascribed to the atrophy of the thymus gland with age and therefore the depressed production of T-lymphocytes (Tasota *et al*., 1998: Online).

Ciliary action and the cough reflex are reduced in the elderly, putting them at high risk. The elderly also have a higher incidence of chronic diseases, making them more susceptible to nosocomial infections. Chronic conditions like chronic lung disease, chronic renal failure and diabetes may be present in the elderly and predispose them more for nosocomial pneumonia (Tasota *et al*., 1998: Online).

3.2.1.2. Smoking

It is common knowledge that smoking attributes to lung diseases, not excluding ventilator-associated pneumonia. Host-related risk factors increase oropharyngeal and gastric colonization (Harris & Miller, 2000:55). Colonization in the smokes will therefore increase the risk for the development of ventilator-associated pneumonia. From experience, males are more often smokers than females (Craven and Steger, 1995:5S). That is why data regarding gender was collected, as it may be one of the risk factors for the development of ventilator-associated pneumonia.

3.2.1.3. Dental plaque

Poor mouth hygiene is often noticed in the patient admitted to the intensive care unit. Before admission, particular health problems e.g. neurological conditions, immobility etc. attribute to the inability of the patient to care for themselves.

The critically ill patient is more exposed to the development of dental plaque due to the difficulty in oral hygiene, changes in salivary properties and changes in oral flora as a result of antibiotic therapy (Harris & Miller, 2000:55). Bacterial colonization of

dental plaque has been implicated as a source of the pathogen in ventilator-associated pneumonia (Kollef, 1999:632).

Fourrier, Duvivier, Boutigny, Roussel-Delvallez, and Chopin (1998:305, 307) found colonization of dental plaque in about 40% of intensive care patients and was associated with an increase in intensive care stay with more than 10 days. This colonization was highly predictive of the subsequent nosocomial infection. The colonization did not only include bacteria, but also yeasts. They also indicated that dental colonization might be due to gastric colonization. Their conclusion was that dental plaque must be considered as a reservoir for colonization and subsequent nosocomial infection in intensive care patients (Fourrier *et al.,* 1998:308).

3.2.2. Chronic diseases

The presence of pre-existing diseases may cause more susceptibility to ventilator-associated pneumonia (Young & Ridley, 1999:1188).

3.2.2.1. Chronic obstructive pulmonary disease

Lynch (3001:375S) mentions that chronic obstructive pulmonary disease is associated with high mortality in the case of ventilator-associated pneumonia. These patients are often exposed to frequent use of antibiotics.

3.2.2.2. Cardiopulmonary, renal, liver, neurological diseases and diabetes mellitus

Patients with the following diseases are at higher risk for the development of ventilator-associated pneumonia: immune-compromised, chronic heart or lung disease, alcoholism or cirrhosis and diabetes mellitus. In these types of patients, surgical procedures may be indicated. The following procedures are also identified as high risk factors in the development of ventilator-associated pneumonia: undergoing thorax or abdominal surgery, have a decreased level of consciousness or instrumentation of the respiratory tract (Thompson, 1995:696).

Some associated conditions like acute respiratory distress syndrome often complicate the diagnosis and management of the patient with ventilator-associated pneumonia. The findings of Chastre, Trouillet, Vuagnat, Joly-Guillou, Clavier, Dombert & Gibert (1998:1172) proved micro-biologically that ventilator-associated pneumonia is a common complication of acute respiratory distress syndrome.

Other conditions associated with gram-negative organisms are diabetes mellitus, malnutrition, renal failure, neoplasms, liver disease, pulmonary edema and other lung pathologies (Young & Ridley, 1999:1188).

3.2.2.3. Compromised immune system

Due to the increasing number of HIV positive and AIDS patients, the care of this high-risk group of patients has been increasing in intensive care units. The lung is often the site of infection in these patients. Pneumonia in these patients is often caused by bacterial infections and *S aureus* and *P aeruginosa* are common causative organisms. These patients are at higher risk of contracting or transmitting respiratory pathogens like pneumococcus, *H influenzae, M tuberculosis and even Pneumocystis carinnii* in the hospital. Outbreaks of penicillin-resistant pneumococci have been experienced in South Africa and Spain. The incidence of *Mycobacterium tuberculosis* in HIV positive patients is as high as 70 to 93%. AIDS patients may even have a negative tuberculin skin test HIV when positive (Craven & Steger, 1995:10S-11S). The Centers for Disease Control and Prevention recommend early identification, prompt (reversed, protective) isolation for these patients and effective therapy.

Another concern is *P carinnii* pneumonia. This organism may spread from person-to-person. Interventions like sputum induction, bronchoscopy, or aerolozed pentamide, increase the risk of nosocomial transmission of *P carinnii* pneumonia (Craven & Steger, 1995:11S).

The immune compromised patient does not present with the typical signs of pulmonary infection, like cough, sputum production, pyrexia and leukocytosis and the

diagnosis is therefore only made much later in the disease process (Albert, Spiro & Jett, 1999:24.3).

3.2.2.4. Alcoholism

Klebsiella pneumoniae ventilator-associated pneumonia is usually seen in the patient diagnosed with alcoholic cirrhosis (Thompson, 1995:696).

3.2.3. Complications of specific conditions

Complications of the specific condition will increase the risk for the development of ventilator-associated pneumonia. These conditions will be discussed below.

3.2.3.1. Acidosis

Severe metabolic imbalances often lead to the development of acidosis, be that respiratory or metabolic or even a combination of the two. This leads to alterations in local and systemic immune response to invading microorganisms (Harris & Miller, 2000:54).

3.2.3.2. Altered level of consciousness

Girou, Stephan, Novara, Safar and Fagon (1998:1155) found a high risk factor for the development of nosocomial pneumonia in patients with neurological failure specifically on day 3. Other researchers found coma, head injury and the presence of neurological disease on admission, to be associated with nosocomial infections (Girou *et al.,* 1998:1157). The association between coma and nosocomial infections is not clear.

3.2.3.3. Severity of illness

It was found in the post-mortems of young healthy individuals, that the predominant organism present in the pulmonary parenchyma was oropharyngeal flora and infrequently aerobic gram-negative bacteria, which was not true in the case of 62% of hospitalized patients. Gram-negative bacteria increase with the severity of the illness, like in the case of coma, respiratory tract disease, hypotesion, tracheal

intubation, acidosis, uremia and either leucocytosis or leucopenia (Young & Ridley, 1999:1188).

The more severely ill the patient becomes, the more energy becomes depleted and the body cannot sustain normal function like maintaining immune function. The critically ill are therefore more susceptible to colonization of exogenous organisms as well as overgrow of endogenous microbes (Tasota *et al*., 1998: Online).

Lynch (2001:375S) identifies the following factors attributing to the severity of the illness that is associated with mortality: advanced age, use of corticosteriods, the presence of shock, late-onset ventilator-associated pneumonia and chronic obstructive pulmonary disease.

3.2.3.4. Response to physical and psychological stress

Physical stressors lead to stimulation of the "fight and flight" response and it does not matter if the response is physical of psychological. Stressors include pain, illness, anxiety, lack of sleep, noise, discomfort and many more. (This is an accurate description of the intensive care environment.) This leads to excessive stimulation of the sympathetic nervous system, which has a negative effect on the neuro-endocrine system by suppressing lymphoid tissue. An elevated level of the cortisol hormones depresses the immune function, synthesis of antibodies, the number of lymphocytes and macrophage. The effectiveness of the function of the leukocytes is also reduced. As the condition worsens, infection can lead to circulatory collapse (Tasota *et al.,* 1998: Online).

Stress leads to changes in the normal barriers of the body, like secretion of salivary proteases that leads to decay of fibronectin. Gram-negative organisms can colonize due to above-mentioned (Tasota *et al.*, 1998: Online).

3.2.3.5. Malnutrition

A hypermetabolic state develops in the critically ill patient due to physical and psychological stressors. This leads to a reduction in production of immune cells in the patient. The reduction in production of immune cells suppresses the host's defense mechanisms (Tasota *et al*., 1998: Online).

Smulders *et al*. (2002:859) lists the following as risk factors for the development of ventilator-associated pneumonia: previous surgery, trauma and a history of chronic obstructive pulmonary disease. These are conditions associated with malnutrition. Chronic conditions are also associated with poor nutrition. Lynch (2001:375S) identifies low albumin levels on hospital admission, as a high risk factor, but is not assessed in this study.

3.2.3.6. Sleep deprivation

The quantity and the quality of sleep in the critically ill patient are disturbed, due to loss of the normal progression through the normal sleep cycle. This adds to the stress of the patient and it may alter immune function. It has been found that interleukin-1, which amplifies the immune response, is suppressed in the presence of abnormal sleep patterns. The secretion of other substances like interleukin-2, natural killer cells, and lymphocyte-activated cells, are released in the presence of sleep deprivation. This may lead to a decline in resistance against infection (Tasota *et al*., 1998: Online).

3.2.4. Trauma

A patient may experience different of which the following are directly associated with ventilator-associated pneumonia: burn trauma, severe head injury and chest trauma.

3.2.4.1. Burn trauma

According to Ellstrom (1999:416) burn patients are at the highest risk of developing ventilator-associated pneumonia. The trauma patient is at high risk of aspiration that could lead to the development of pneumonia.

3.2.4.2. Severe head trauma

A depressed level of consciousness, as found in head trauma, was also evidenced as significantly predisposing to the development of pneumonia. Neurological dysfunction may be a marker of impairment of the host's defenses. Coma, head trauma and neurological disease present on admission, were found to be associated with nosocomial infection (Girou *et al.,* 1998:1157).

3.2.4.3. Chest trauma

There are a few factors that increase the chest trauma patient's risk of the developing of ventilator-associated pneumonia. The first is that the patient may aspirate during and after trauma. The second fact is that the patient's coughing may be impaired as a result of pain (Harris & Miller, 2000:55). The contusion of the lung itself makes the patient more susceptible to the development of ventilator-associated pneumonia.

3.3. TREATMENT-RELATED FACTORS

Some medical and nursing procedures increase the risk for the development of ventilator-associated pneumonia, as they decrease the host's defenses and increase the exposure to organisms (Harris & Miller, 2000:56). Girou *et al.* (1998:1157) adds to this list a persistently high level of therapeutic activity as a high risk factor for the development of nosocomial infections.

3.3.1. Endotracheal intubation and mechanical ventilation

"The most significant risk factor for developing a hospital-acquired pneumonia is tracheal intubation" (Tasota *et al*., 1998: Online). The risk for development of a nosocomial infection increases every time that invasive method bypasses the normal defense mechanisms (Tasota *et al*., 1998: Online). Examples of invasive devices are endotracheal tubes, indwelling catheters and urinary catheters.

3.3.1.1. Endotracheal intubation

Intubation with an endotracheal tube can directly and indirectly attribute to ventilator-associated pneumonia. One of the direct cases is that the endotracheal tube makes

direct contact with the inner wall of the trachea. This direct contact causes **mucosal damage** that reduces mucocilliary function (Grap & Munro, 1997:420). In addition the endotracheal tube bypasses the upper airway defense mechanisms. The problem is enhanced by the fact that the endotracheal tube leads to **ineffective coughing mechanism** (Grap & Munro, 1997:420). The endotracheal tube does not allow for closure of the vocal cords during coughing.

The endotracheal tube indirectly attributes to ventilator-associated pneumonia as it acts as a **binding site** for organisms (Grap & Munro, 1997:420). This will contribute to the colonization of organisms in the upper airway. The endotracheal tube is a foreign object to the body and therefore causes the increase in mucus production. These secretions are an excellent medium for the growth of pathogens. The body's normal defense mechanisms cannot reach the organism on the surface of the endotracheal tube (Grap & Munro, 1997:420).

Nasotracheal intubation

Some studies indicate that nasotracheal intubation increases the risk for maxillary sinusitis, but other researchers found no significant difference in the rate of maxillary sinusitis between patients intubated orally or nasally (Grap & Munro, 1997:420). However, according to Kollef (1999:631) nosocomial sinusitis may predispose a patient for developing pneumonia as the secretions from the sinuses may be aspirated. The preferred route of intubation is oral (Eggiman & Pittet, 2001:2078; Kollef, 1999:630).

3.3.1.2. Mechanical ventilation

It is impossible to separate the risk factors associated with intubation and mechanical ventilation as they are so closely related. The mechanical ventilator does not directly lead to pneumonia, but the process of intubation, devices and procedures linked to the mechanical ventilation do increase the risk. These aspects will be discussed under infection-control related risk factors.

Endotracheal intubation for longer than 48 hours can lead to the development of ventilator-associated pneumonia. Pneumonia may even develop before 48 hours in the case of: large volume aspiration, sedation, decreased level of consciousness, Glasgow coma scale rating less than 9, emergency procedure, cardiopulmonary resuscitation and respiratory/cardiac arrest as cause of intubation (Lynch, 2001:375S).

Some studies also identified the following as risk factors: high positive end-expiratory pressure, absence of antibiotic therapy, upper respiratory tract colonization by gram-negative bacilli, extended duration of mechanical ventilation (Lynch, 2001:375S). All these factors are associated with the patient receiving mechanical ventilation.

3.3.1.3. Reintubation and self extubation

Reintubation is also associated with a higher risk of developing ventilator-associated pneumonia. The patient who requires reintubation has six-fold probability of developing ventilator-associated pneumonia (Grap & Munro, 1997:421).

Aspiration of subglottic secretions or gastric content in the case of self- or accidental extubation is considered to be the cause of ventilator-associated pneumonia. In the case of too early extubation, the patient may be unable to maintain his airway (especially in the neurosurgical patient) due to glottic dysfunction (Torres, Gatell, Aznar, El-Ebiary, Puig de la Bellacasa, Gonzálles, Ferrer & Rodriquez-Roisin, 1995:140).

3.3.2. Devices and their complications

Devices like nasogastric tubes, intracranial monitor catheters and bronchoscopes have their individual complications that may increase the risk for the development of ventilator-associated pneumonia.

3.3.2.1. Nasogastric tubes

The presence of nasogastric tubes increases the risk for the development of ventilator-associated pneumonia with rates ranging from 0.8% to 77% (Grap & Munro, 1997:421). The presence of nasogastric tubes leads to stagnation of oropharyngeal secretions because the presence of the tube impairs swallowing. The nasogastric tube also leads to reflux of gastric content and acts as a conduit for bacteria up from the stomach to the oropharyngeal space (Harris & Miller, 2000:56). Writers indicate that large bore tubes do not cause more reflux than small bore nasogastric tubes (Young & Ridley, 1999:1191).

Organisms attached to the surfaces of these devices are out of reach of the effect of antibiotics and body defenses. Organisms can be mobilized to the lower respiratory airways by high pressures and turbulent flow during ventilation (Thomson, 1995:698).

3.3.2.2. Enteral feeding increases gastric pH

Enteral feeding leads to both increased pH of the stomach and gastric colonization (Harris & Miller, 2000:56). Both bolus and intermittent enteral feeding is associated with colonization of the stomach with gram-negative bacteria. However, adequate nutrition is essential in the prevention of ventilator-associated pneumonia and enteral feeding has been shown to be the route of choice (Young & Ridley, 1999:1191).

Gastric reflux and aspiration of enteral feeds

In the presence of a nasogastric tube, esophageal reflux may take place. This contributes to the migration of organism up the nasogastric tube (Grap & Munro, 1997:427). In the prevention of this complication, percutaneous jejunostomy tubes or nasogastric tubes positioned in the jejunenum may be used. Increased gastric volumes may increase reflux (Harris & Miller, 2000:56). Continuous, rather than intermitted enteral feeding regimes are used to prevent such complications.

Over distention of the stomach should be monitored (Young & Ridley, 1999:1191). Causes of overdistention are the use of narcotics and anticholinergic agents. The

use of these substances, monitoring gastric residual volumes after gastric feedings and using agents to improve motility will reduce the possibility of aspiration. Other interventions to be considered are using small-bore feeding tubes and feeding into the small bowel rather the stomach (Kollef, 1999:630). These interventions should still be confirmed with clinical trials. In general, the patient with a paralytic ileus is at greater risk for aspiration (Mahul *et al*., 1992:23).

3.3.2.3. Aspiration, microemesis and microaspiration

During sleep, 45% of normal persons aspirate (Harris & Miller, 2000:53) however they do not develop pneumonia. This is attributed to the size, the nature of the inoculum, and the defense capabilities of the defense mechanism. It has also been found that the rate of aspiration in patients with a depressed level of consciousness is as high as 70%. These patients have impaired airway reflexes and are at higher risk of developing pneumonia (Harris & Miller, 2000:53). This type of patient may aspirate before intubation, which may lead to ventilator-associated pneumonia after intubation. This is often seen in the neurosurgical patient as their level of consciousness decreases due to neurological complications.

In the past, the cuff of the endotracheal tube was thought to prevent aspiration, but the opposite has been found. Secretions accumulate on top of the cuff in the subglottic space and leak between the cuff and the tracheal wall. It was found in 87 to 100% of cases that when dye was placed in the subglottic space, it passed between the cuff and the wall of the trachea. The folds that the cuff of the endotracheal tube form as it is inflated facilitate this leakage. Even when the cuff pressure was increased above normal limits in cadaver studies, the leakage continued and the rate was at a few milliliters per minute (Young & Ridley, 1999:1189). “The high-volume, low-pressure cuff of a tracheal tube does not prevent the leakage of potentially infected fluid from the subglottis to the trachea” (Young & Ridley, 1999:1189). This means that the patient may be exposed to aspiration even after intubation and the endotracheal cuff should not be considered as a means against aspiration.

3.3.2.4. Presence of intracranial pressure monitor

The presence of an intracranial pressure device makes the handling of the patient difficult and leads to the reluctance to turn the patient due to fear of displacement of these devices (Harris & Miller, 2000:55).

3.3.2.5. Bronchoscopy

The role, which the bronchoscope plays in the development of ventilator-associated pneumonia, is that it is difficult to properly clean these devices. Therefore organisms can be carried in the device from one patient to the next, causing contamination of the patient's lower airways.

3.3.3. Medical treatment

The purpose of medical treatment is to improve the condition of the patient. However, these treatments may also increase the risk of developing ventilator-associated pneumonia.

3.3.3.1. Indiscriminate use of antibiotic therapy

Indiscriminate and prior antibiotic use is associated with higher incidence of nosocomial infections and it leads to antibiotic-resistant strains (Grap & Munro, 1997:420). Patients previously exposed to antibiotics are at higher risk of developing ventilator-associated pneumonia (Kollef, 1999:632). Indiscriminate prescription of antibiotics leads to the destroying of normal flora and allowing colonized pathogens to overgrow. The physician is usually under pressure to prescribe antibiotics, due to factors like: pressure from pharmaceutical companies and the severity of the infection without the benefit of identification of the causative organism.

3.3.3.2. Broad-spectrum antibiotic use

In some cases broad-spectrum antibiotics are prescribed, where narrow spectrum antibiotics are indicated. In some cases the patient may even present with the

symptoms of an infection due to physiological reaction of the body to surgical or invasive procedures (Tasota *et al*., 1998: Online).

Antimicrobial therapy is a complex subject, but the critical care nurse should be aware of problems associated with this topic.

3.3.3.3. Therapy elevating gastric pH

The patient receiving mechanical ventilation is at higher risk of developing upper gastrointestinal hemorrhage and therefore requires preventive therapy (Kollef, 1999:631). In the prevention of the development of stress–induced gastritis, gastric alkalization is sometimes used. The increase in gastric pH promotes bacterial colonization of the stomach, particularly gram-negative organisms (Grap & Munro, 1997:421). (The writers also indicate other studies that did not confirm this phenomenon). The type of organisms that colonize can be gram-positive bacteria, gram-negative bacteria and yeasts. On aspiration of stomach content the patient develops nosocomial pneumonia (Tasota *et al*., 1998: Online).

3.3.3.4. Histamine$_2$-receptor antagonists

Another important factor pointed out was that histamine$_2$–receptor antagonists decreased incidence of gastrointestinal bleeding. The incidence of nosocomial pneumonia was lower in subjects that received sucralfate, compared to those that received antacids or histamine$_2$–receptor antagonists. There was a reduction in the mortality rate in those that received sucralfate (Tasota *et al*., 1998: Online; Young & Ridley, 1999:1191).

3.3.3.5. Selective gastrointestinal decontamination

Selective decontamination of the oropharynx and the gut with topical nonabsorbable bactericidal antimicrobials, reduced colonization rates resulting in a increased incidence of lower respiratory tract infections. However, there was not any change in the mortality of the subjects (Young & Ridley, 1999:1191).

In some studies, selective decontamination of the digestive tract was used to reduce the incidence of ventilator-associated pneumonia. It was found that the incidence of pneumonia was reduced. However, it was not clear if the morbidity and mortality rates were reduced. The concern still remains that the development of multi-resistant strains of organisms is possible (Grap & Munro, 1997:422). At this research site, selective decontamination of the digestive site is not practiced, due to the previously mentioned concerns.

3.3.3.6. Head surgery

The factors that attribute to ventilator-associated pneumonia, in the patients undergoing head surgery, are firstly that these patients have a depressed level of consciousness due to the neurological condition, as well as the use of anaesthetics, sedatives and analgesia. These patients are usually positioned supine at 20^{O} head and thorax lifted. This increases the risk for aspiration. These patients can become restless and self-extubate (see 3.3.1.3). Intracranial pressure monitoring may also be utilized and is in itself a risk factor (see 3.3.2.4.)

3.3.3.7. Upper abdominal surgery or thoracic surgery

The patient who undergoes abdominal or thoracic surgery is at risk for the development of ventilator-associated pneumonia due to the pre-existing condition that may lead to malnutrition, long hospitalization and therefore exposure to pathogens. These patients may experience pain post-operatively that will lead to depression of ventilation and coughing. These are factors that can lead to ventilator-associated pneumonia. These patients are usually nursed in a supine position, due to haemodynamic instability and for comfort of the patient.

3.3.3.8. Supine position

The semi-recumbent position (45^{0} elevation of the head and thorax) seems to reduce aspiration, compared to the supine position (Bowton, 1999:30S). However, the neurosurgical patient is positioned at 20^{0} to maintain cerebral perfusion and to reduce intracranial pressure (Hickey, 1997:323).

Another factor to be considered is the time that a patient spends in the supine position. Usually the critically ill patient is kept in a supine position for longer periods. Both the supine position and the time spent in the supine position, are listed as risks. The patient with a nasogastric tube, receiving enteral feeding in the supine position combination is considered to be at high risk for aspiration factors (Harris & Miller, 2000:56). During surgery some neurosurgical patients are positioned supine for at least three hours.

3.3.3.9. Immunosuppressive agents

One of the drugs that lead to the suppression of the immune system and which is applicable to this research, is dexamethasone. This drug is used to reduce cerebral oedema in the post surgical phase. Dexamethasone suppresses the endogenous cortisol production (Gibbons & Swanepoel, 1995:212).

3.3.3.10. Inadequate pain control

Inadequate pain management will lead to ineffective breathing, coughing and reduction in movement.

3.4. INFECTION CONTROL-RELATED FACTORS

Under infection control-related factors, transgression of the infection control principles and respiratory equipment-related issues will be covered.

3.4.1. Transgression of infection control principles

Cross-contamination is one of the role-players in the spreading of nosocomial infections. Gram-negative organisms are present in all hospitals. Microorganisms are present in the critically ill patient and on the hands of those who care for them (Harris & Miller, 2000:56).

3.4.1.1. Poor hand washing techniques

When talking about hand washing, everybody testifies to its importance. When asked if they do perform it, medical and nursing staff know when to wash their hands. But when directly observed, the actual performance of hand washing is very limited. According to Grap and Munro (1997:420) the average time spent on hand washing is 8.6 seconds, in contradiction with the 10 seconds suggested by the Centers of Disease Control and Prevention. (The local policy at the research site is 15 seconds for a social wash procedure and 2 minutes for the scrubbing procedure.) Studies showed that only 41% of health workers and 28% of physicians in an ICU washed their hands after patient contact. Nursing staff reports 90% of compliance to hand washing, but the observed rate was only 22% (Tasota *et al*., 1998: Online).

Hands should be washed before and after touching a patient. The effectiveness of hand washing to prevent nosocomial infections, has been proven since the days of Florence Nightingale. It still remains a cheap and effective measure in the battle against nosocomial infections (Tasota *et al*., 1998: Online).

Many excuses are offered by the nursing staff for none compliance with hand washing guidelines. This brings up the ethical question in such statements, as nurses are the primary advocates of the critically ill patient and should not compromise patient care. Excuses that have been offered are “I am too busy” and “skin irritation due to cleaning agents”. Measures to improve hand washing can includes sinks installed closer to the patients, less irritating cleaning agents and infection control education (Tasota *et al*., 1998: Online).

Most pathogens can survive up to 30 minutes on the hands. By washing the hands regularly the number of pathogens will be reduced significantly. Adherence to a good hand washing procedure will ensure that the health care workers do not acquire infections themselves (Tasota *et al*., 1998: Online).

3.4.1.2. Poor suctioning techniques by care givers

If staff does not adhere to stringent aseptic techniques, contamination of the lower respiratory tract may occur during endotracheal suctioning. The issue is actually more complex, as biofilms containing bacteria like gram-negative bacteria and *Staphylococcus aureus,* rapidly adhere to the inner lumen of the endotracheal tube. These organisms may be propelled into the trachea and lower airways by shear forces of gas flow and passing suction catheters (Young & Ridley, 1999:1189) and therefore by devices like bronchoscopes. Just by passing a suction catheter down the endotracheal tube, 60 000 viable colonies of bacteria may be dislodged by instilling of saline, which is a normal practice in the suctioning procedure, 310 000 colonies of bacteria may be dislodged (Tasota *et al*., 1998: Online).

The closed multi-use catheter system was designed to prevent breaking of the closed system and therefore prevent contamination during the suctioning procedure. The benefit that it showed is that it prevented desaturation and arrhythmias in the patient, during the suctioning procedure (Cook *et al*., 1998:786). "However, there was no difference in the ventilator-associated pneumonia rates with closed, as opposed to open, tracheal suction systems " (Young & Ridley, 1999:1189). The cost of these devices is significantly higher than the open single-use suction catheter system. It also has to be considered that the open single-use catheter system is associated with the use of many other types of equipment and consumables.

The benefit of the multi-use catheter system is associated with fewer suction-induced complications, disturbances in arterial pressure, heart rate and rhythm and oxygenation. The multi-use catheter system was also considered to be cost effective (Johnson, Kearney, Johnson, Niblett, MacMillan & McClain: 1994:665).

In an interesting study, Kollef, Prentice, Shapiro, Fraser, Silver, Trovillion, Weilitz, Von Hartz and St. John (1997:471) have demonstrated that the practice of not routinely changing closed multi-use catheter systems during mechanical ventilation is safe and cost-effective, compared to daily changes. Suction catheters were only changed in

the case of disconnection of the ventilator circuit e.g. the patient went to theatre. The closed multi-use catheter system was also changed when visibly soiled.

3.4.1.3. Understaffing

Routine strategies in the prevention of nosocomial infections may decline as the patient-to-nurse ratio increases. Strategies in the prevention of ventilator-associated pneumonia like turning the patient, suctioning, complying with infection control and aseptic measures may decline (Tasota *et al*., 1998: Online).

3.4.2. Respiratory equipment-related issues

The main mechanism of contamination of respiratory equipment is still attributed to endogenous bacteria from the stomach or oropharynx leaking past the endotracheal cuff and then subsequently contaminating the endotracheal tube and the ventilator circuit as the patient coughs (Young & Ridley, 1999:1189). This also applies to nebulizers, resuscitation bags and humidifiers.

3.4.2.1. Respiratory equipment contamination and spillage

The ventilator circuit consists of the components between the ventilator and the endotracheal tube. The ventilator circuit includes the following components: delivery tubing, monitor tubes, medication delivery systems, monitoring probes, ventilator exhalation valves, water traps expiratory tubing and humidifier. Any break in the closed system can lead to access for a pathogen to the airway of the patient (Mathews & Mathews 2000:18).

Opinions may differ on the role of ventilator circuits' in causing ventilator-associated pneumonia. According to Young and Ridley (1999:1198) respiratory equipment may directly play a role in contamination of the lower airways due to cross-contamination or inadequate cleaning and sterilization procedures. However, this only happens rarely. According to Grap and Munro (1997:421), contaminated respiratory equipment poses a low risk for the development of ventilator-associated pneumonia, even if bubble through or wick humidifiers are used. However, if the inspiratory circuit and its

condensate are contaminated by bacteria from the patient's oropharynx and subsequently is spilled into the tracheobronchial tree, it may lead to ventilator-associated pneumonia (Grap & Munro, 1997:421).
According to Lynch (2001:374S), nebulizers and ventilator tubing have been implicated in epidemics of infections. One can easily add resuscitation bags to this list as it causes breaking of the closed system.

Ventilator circuits become colonized as soon as they are connected to the patient. When the patient aspirates condensate from the ventilator circuit it may lead to the development of a ventilator-associated pneumonia. This is why heat and moisture exchangers are suggested, to prevent the formation of condensate in the circuits. These devices have the ability to filter out bacteria from the inspired air (Bowton, 1999:31S).

Humidifiers

Two types of humidfications are used. The first device, (used in this research) is the heated humidifier. The second types are the heat and moisture exchange humidifier and hygroscopic condenser humidifier, which are filters connected between the endotracheal tube and the ventilator circuit. Both heat and moisture exchange humidifiers and hygroscopic condenser humidifiers trap heat and moisture from the expired gas and release it to the inhaled gas. Humidifiers seem to be effective in reducing ventilator-associated pneumonia in the long term, but lack the humidification to liquefy infected secretions (Mathews & Mathews, 2000:19). The endotracheal tube bypasses the normal humidification mechanism and humidification has to be supplemented.

The heated humidifier was chosen for this research due to the reduced rate of endotracheal tube blockages, compared to the heat and moisture exchange humidifier.

Heat and moisture exchange humidification has an advantage above the first mentioned device, as it prevents ventilator tube condensate from running down in the endotracheal tube. Ventilator tube condensate frequently has high bacterial counts (Young & Ridley, 1999:1190). These contaminated fluids can drain into the patient's airway and cause a ventilator-associated pneumonia (Mathews & Mathews, 2000:18).

To solve this problem in the research, ventilator circuits with heater wires were selected and circuits with water traps. The function of the heater wire is to reduce condensation in the ventilator circuit as it prevents the cooling of the oxygen that leads to condensation of the water in the ventilator circuit. Heated wires are electrical wires that run in the ventilator circuit from the humidifier to the patient connector (Mathews & Mathews, 2000:19).

Medication nebulizers

Nebulizers can be either high frequency sound wave or pneumatically driven, to brake down the size of the liquid (Mathews & Mathews, 2000:19). Nebulizers have no heating properties. The nebulizers saturate the inspiratory gas with water or the medication added. The use of nebulizers indicate that the closed system of the ventilator circuit must be broken every time this therapy is applied and may be contaminated in the process, leading to the contamination of the ventilator circuit and the lower airways, eventually.

In the case where nebulizers are contaminated, bacteria may enter the lower respiratory tract. The size of the aerosol determines how far it will travel. The smaller the aerosol, the further it will travel and may therefore bypass the natural defense mechanisms. The smaller the contaminated aerosol, the higher the risk for the development of pneumonia (Harris & Miller, 2000:55). Craven, Lichtenberg, Goularte, Make and McCabe (1985:835) have found a high incidence of gram-negative colonization on nebulizers, when only cleaned once in 24 hours and a reduction if nebulisers where cleaned after every use.

As many as 68% of repeatedly used nebulisers are contaminated with high levels of organisms (>10^3.ml^{-1}). It is advised that nebulisers should be disposed of, as cleaning of the nebulisers only reduced the contamination with 20% (Young & Ridley, 1999:1190).

3.4.2.2. Changing of ventilator tubing more often than every 48 hours

The Centers for Disease Control and Prevention in 1994 recommended changing of ventilator circuits every 48 hours or longer. Due to improvement of designs some hospitals change of ventilator circuits every 5 days (Mathews & Mathews: 2000:18). The Centers for Disease Control and Prevention do not give any recommendations regarding the maximum length of ventilator circuit use.

Randomized trials showed that the frequency of ventilator circuit changes had little influence on the rate of ventilator-associated pneumonia. Infrequent changes were in fact associated with a moderate decrease in ventilator-associated pneumonia rate. A 7 and 30-day circuit change intervals there was lower risk of ventilator-associated pneumonia, than 2-day change intervals. This was attributed to the more frequent manipulation of the endotracheal tube. The handling led to the leaking of contaminated secretions past the cuff of the endotracheal tube (Young & Ridley, 1999:1189).

3.5. CONCLUSIONS

Risk factors are divided into host-related, treatment-related and infection control-related. The critical care nurse must be on alert to identify risk factors for the development of ventilator-associated pneumonia. This will assist in the implementation of preventative strategies. The development of a risk factor assessment tool is warranted. This will assist in the early recognition of high risk patients. The critical care nurse can play an active role in the identification of the elements for such an instrument.

CHAPTER 4
LITERATURE REVIEW
PREVENTATIVE STRATEGIES IN VENTILATOR-ASSOCIATED PNEUMONIA

4.1. INTRODUCTION

When investigating guidelines in the prevention of ventilator-associated pneumonia, some misleading opinions are often offered. In the case of multiple studies on related problems, the findings are even contradictory (Grap & Munro, 1997:425). Recommendations by the Centers for Disease Control and Prevention have always been the major guideline.

The Hospital Infection Control Practices Advisory Committee (HICPAC) of the Centers for Disease Control and Prevention drew up guidelines for the prevention of ventilator-associated pneumonia. The HICPAC guidelines categorize recommendations based on existing scientific evidence as well as the economic impact, as some suggested interventions are not based on research. The only concern with these guidelines is that the last revision was in 1997. These guidelines were revised and published in 2003 (Tablan *et al*., 2004: Online). The structure of these guidelines is similar to this chapter (compiled before the Centers for Disease Control and Prevention guidelines of 2003.

4.1.1. Education

According to the Centers for Disease Control and Prevention, education of medical staff is the foundation in the prevention of nosocomial infections. Staff should be trained regarding the pathogeneses, risk factors and effective preventative strategies of ventilator-associated pneumonia (Harris & Miller, 2000:57).

4.2. RISK FACTORS

The strategies to be addressed will be covered with the same structure of the risk factors in Chapter 3. The main strategies will again be divided into host-related, treatment-related and infection control-related. The critical care nurse should be able to recognize risk factors that can be addressed (Harris & Miller, 2000:57).

Table 4.1 Risk factors that can be addressed

STRATEGIES TO ADDRESS RISK FACTORS
HOST-RELATED strategies
Patient characteristics ❑ Dental plaque ❑ Immune system enhancement therapy ❑ Vaccines
Limiting the complications of the condition: ❑ Prevention of aspiration ❑ Optimal nutrition ❑ Limiting physical and psychological stress ❑ Limiting sleep deprivation
TREATMENT-RELATED STRATEGIES
Endotracheal intubation and mechanical ventilation ❑ Oro vs. naso-tracheal intubation ❑ Subglottic suctioning ❑ Cuff pressure management ❑ Reduce unplanned extubation ❑ Noninvasive ventilation
Devices and their complications ❑ Nasogastric tubes ❑ Enteral feedings

STRATEGIES TO ADDRESS RISK FACTORS
Medical treatment
❑ Appropriate antimicrobial therapy ▪ Prophylactic antibiotics ▪ Empirical antimicrobial therapy ▪ Prophylactic treatment of patients with neutropenia ▪ Correct antimicrobial therapy in the presence of ventilator-associated pneumonia ▪ Monotherapy and combination therapy ❑ Maintain a low gastric pH ❑ Positioning of the patient ▪ Kinetic beds and postural changes ▪ Semi-recumbent position of the patient ▪ Early mobilization Pain control
INFECTION CONTROL-RELATED STRATEGIES
Improvement of infection control principles
❑ Standard/ universal precautions ▪ Hand decontamination ▪ Gloves ▪ Masks ▪ Gowns or plastic aprons ***Management of respiratory equipment related issues*** ❑ Ventilator circuits ▪ Changing of ventilator circuits ▪ Continuous management of ventilator circuits ❑ Pulmonary secretions ▪ Open single-use vs. closed multi-use catheter systems ▪ Physiotherapy ❑ Heated and heat and moisture exchange humidifiers

4.3. HOST-RELATED FACTORS

Host related factors address two main issues e.g. certain patient characteristics and how to limit the complications of the condition. Some of the listed host-related risk factors (Table 3.1) such as, age, severity of illness, pre-existing diseases, can unfortunately not be manipulated.

4.3.1. Patient characteristics

Factors related to patient characteristics that can be addressed are dental plaque, immune system enhancement therapy and vaccines.

4.3.1.1. Dental plaque

Antimicrobial therapy may change oral flora in the critically ill patient that can lead to colonization of the saliva (Harris & Miller, 2000:57). This can lead to the colonization of dental plaque. Dental plaque has been implicated as a source of ventilator-associated pneumonia (Kollef, 1999:632).

Since 1959, dentists controlled dental plaque by using chlorhexidine. The use of chlorhexidine has been shown to be effective in reducing ventilator-associated pneumonia in patients undergoing cardiac surgery. The administration is done with ease and is advised in high-risk patients. Overuse may lead to colonization, superinfections and chlorhexidine-resistance (Kollef, 1999:632).

“The use of oral chlorhexidine rinse in cardiac surgical patients reduced postoperative respiratory infections by 69%, and subsequently reduced antibiotic use. Antibiotic resistance was unaffected” (Young & Ridley, 1999:1190). In above-mentioned study, chlorhexidine gluconate 0.12% was performed only twice a day in cardiac surgery patients. This treatment is quite inexpensive (4cents per treatment) and easily administered compared to the administration of antimicrobial therapy (Deriso, Ladowski, Dillon, Justice, & Peterson, 1996:1559).

Studies should still be clear on the type and frequency of oral hygiene required to decrease colonization and therefore prevent ventilator-associated pneumonia (Harris & Miller, 2000:57).

The toothbrush has been recommended as the ideal tool to remove plaque from the patient’s teeth. However the critical care nurses do not often select the toothbrush as

a tool for mouth care and will rather select other devices like gauze etc. The writer suggests that a soft baby brush can be used in the intensive care setting. After three days of neglected mouth care, hundreds of species of bacteria, including gram-negative bacteria become more prevalent (Kite & Pearson, 1995:71, 75).

The frequency for mouth care in this study is six hourly. Mouth rinses are performed with Hibident® solution (chlorhexidine gluconate 2%). From my own experience and from literature, oral care in the critically ill patient is often neglected.

4.3.2. Immune system enhancement therapy

Immunoglobulin therapy and vaccines will be discussed under this heading. Unfortunately, these strategies are not applicable for all ventilated patients.

4.3.2.1. Immunoglobulin therapy

The use of intravenous administration of immunoglobulin has been proven to reduce the incidence of ventilator-associated pneumonia in 50% of cases when administered to high-risk subjects. However these types of drugs are very expensive and the practice is presently only experimental (Kollef, 1999:632; Young & Ridley, 1999:1193).

4.3.2.2. Vaccines

Various vaccinations are available and are used to reduce pneumonia. To be effective, this type of therapy should be administered before admission to the hospital. Vaccination can also be included into a discharge program for patients at high risk of developing respiratory infections (Kollef, 1999:633).

The Centers for Disease Control and Prevention recommends that high-risk patients should receive vaccination for influenza and pneumococcal infections. The recommendations also include the annual vaccination of health workers (Thompson, 1995:699).

4.3.3. Limiting the complications of the condition

The critical care nurse can play an active role in early identification of the condition and complications, assessment of the patient and by self-education on updated guidelines in the management of the different conditions.

4.3.3.1. Prevention of aspiration

The World Health Organization (Williams, Sharma, Atukorala, Kelkar, Sharma, Wattanaasri, Lolekha, & Unahalekhaka, 2002:33) emphasizes the prevention of aspiration in the non-intubated, comatose patient by positioning the patient on his/her side. The writers recommended that oral feeds should be avoided in patients with neurological or swallowing abnormalities. They also recommended that sedatives and narcotics should be limited in patients with impaired consciousness.

In this study, patients are nursed pre-intubation with the head elevated at 20 to 30^{o} to reduce raised intracranial pressure. The use of sedatives and narcotics are not so easily avoided in the neurosurgical patient due to restlessness and seizures. However the patient is closely monitored for aspiration.

4.3.3.2. Optimal nutrition

Nutrition in the critically ill is essential in the prevention of ventilator-associated pneumonia. Malnutrition leads to colonization of the oropharynx and the trachea (Harris & Miller, 2000:62). Providing adequate nutrition for the neurosurgical patient is crucial in the healing and recovery process. The caloric requirements of the critically ill patient are two to three times higher in the patient that experiences ongoing stress or serious injury (including surgery) or sepsis (Hickey, 1997:165). The nutritional needs can be assessed by anthropometric measures like height, weight, triceps skinfold thickness, arm muscle circumference and mid-upper arm circumference indicating body fat and lean body muscle (Hickey, 1997:170).

In this study protein and fat composition is assessed by measurement of the triceps skinfold thickness, arm muscle circumference and mid-upper arm circumference.

Malnutrition has a negative effect on the production of surfactant, diaphragmatic mass and vital capacity. This is why it is important to prevent malnutrition, rather than to correct them when they do occur (Thelan, Urden, Lough & Stacy, 1998:133).

Usually critical care departments have access to dietitians that assist in the correct management of the malnourished patient. Enteral nutrition is more effective and cost effective than parental. The problem with enteral nutrition is that it may attribute to aspiration of gastric content (see 3.3.2.2).

In this study nutritional support will be monitored. The practice at the research site is to commence early with nutritional support.

4.3.3.3. Limiting physical and psychological stress

Physical and psychological stimuli, like forced immobilization, trauma, pain, fear, threat of loss, lack of control or anxiety, can cause a multi-system response. These stimuli can be experienced to different degrees (Hickey, 1997:226). The critical care nurse however plays an important role to reduce these stimuli by providing information empathetically, listening skills and by encouragement (Hickey, 1997:227). The patient will go through the stages of grievance; the patient may experience emotions of anxiety, frustration, anger, hostility, fear regression, denial, guilt, depression and feelings of powerlessness (Hickey, 1997:228-231). The key to help the patient is to identify the emotion correctly and to provide support accordingly. This however is difficult when the patient is intubated and can therefore not be done effectively.

4.3.3.4. Limiting sleep deprivation

As already discussed (3.2.3.4), sleep deprivation has a negative effect on the immune system of the patient. The nurse should try to provide a normal uninterrupted sleep period and to remove any obstacles that interfere with it (Hickey, 1997:233).

4.4. TREATMENT-RELATED RISK FACTORS

Treatment-related risk factors address endotracheal intubation and mechanical ventilation, devices and their complications and medical treatment.

4.4.1. Endotracheal intubation and mechanical ventilation

Endotracheal intubation and mechanical ventilation are the main factors that lead to ventilator-associated pneumonia and need addressing. The following aspects will be discussed: oral versus nasotracheal intubation, subglottic suctioning, cuff pressure management, reducing unplanned extubation and noninvasive ventilation.

4.4.1.1. Oral versus nasotracheal Intubation

Prevention of aspiration of gastric content is crucial before, during and after intubation. The most common factor that contributes to aspiration before intubation is depressed level of consciousness. This emphasizes the role of the critical care nurse to recognize the need for airway management in the patient whose level of consciousness deteriorates. Applying cricoid pressure until the patient is successfully intubated can prevent aspiration during intubation (Thelan *et al*., 1998:697).

The incidence of ventilator-associated pneumonia is less in the case of oral intubation than in the case of nasal intubation. This is due to the fact that the incidence of sinusitis was less in the case of oral intubation than nasal intubation (Young & Ridley, 1999:1191).

The general principle at this research site is to intubate patients through the mouth.

4.4.1.2. Subglottic suctioning

Subglottic suctioning will be discussed in full in Chapter 5 as a very important strategy to prevent aspiration. The main aspect for the development of ventilator-associated pneumonia is aspiration of secretions past the cuff. It is important to take any measure to prevent aspiration.

4.4.1.3. Cuff pressure management

Subglottic suctioning will be discussed in the Chapter 5 as a strategy to prevent aspiration.

4.4.1.4. Reducing unplanned extubation

Appropriate securing of the endotracheal tube and prevention of accidental or self-extubation will reduce ventilator-associated pneumonia associated with re-intubation (Young & Ridley, 1999:1192). This will include the appropriate use of physical and chemical restraints and securing of the endotracheal tube (Kollef, 1999:629).

Self-extubation is a high-risk factor for developing ventilator-associated pneumonia. The prevention of self-extubation is therefore crucial (Harris & Miller, 2000:57). In this research, self- or accidental-extubation before 24 hours is a withdrawal criterion.

4.4.1.5. Noninvasive ventilation

Noninvasive ventilation has recently become more popular due to the reduction of ventilator-associated pneumonia (0%) compared to invasive ventilation (28%). The mortality compared in noninvasive ventilation and invasive ventilation was 92% and 72% respectively (Young & Ridley, 1999:1191).

4.4.2. Devices and their complications

Devices that will be discussed are nasogastric tubes inserted for the draining of gastric fluids and enteral feeding.

4.4.2.1. Nasogastric tubes

The size of the nasogastric tube is not an important determinant of gastro-esophageal reflux. Large-bore tubes do not cause more reflux than small-bore tubes (Grap & Munro, 1997:421; Young & Ridley, 1999:1191).

4.4.2.2. Enteral feeding

The prevention of aspiration of gastric content and enteral feeding in the intubated patient is very important in the prevention of ventilator-associated pneumonia.

It is the responsibility of the nurse to assess bowel sounds to determine the risk of reflux and aspiration of gastric content. Symptoms of feeding the patient too much or too rapidly, gastroparesis or gastrointestinal obstruction should be identified promptly.

Aspiration of enteral feeding, due to gastric reflux, is one of the risks associated with enteral feeding. One of the ways to prevent gastric reflux is to position the patient with the head lifted 30 to 45 degrees while enteral feeding is performed (Grap & Munro, 1997:426). This will reduce the risk of aspiration. According to Young and Ridley (1999:1191), there is a four-fold reduction in the incidence of aspiration when patients are positioned at 45^0 angle. "Furthermore the isolation of the same organisms from the stomach, pharynx and endobronchial samples in 32% of semirecombent patients compared to 68% of the supine patients" (Young & Ridley, 1999:1191). An increase in intragastric volume and pressure will lead to gastric reflux. The patient has to be evaluated for gastric distention in the absence of bowel sounds and an increase in residual volume to identify the risk for gastric reflux (Harris & Miller, 2000:62). This will take place in the presence of a paralytic ileus.

Recently, it has been suggested that the nasogastric tube should be positioned distal to the pylorus, but the outcome of research like this has not proven a reduction in nosocomial pneumonia and is still ongoing (Harris & Miller, 2000:63).

In the prevention of aspiration during enteral feeding, the following measures can be taken:

1) keep the head elevated at least at 45 degrees during feedings, unless contraindicated;
2) discontinue feedings 30 to 60 minutes before any procedures that require lowering of the head;

3) keep the endotracheal tube cuff inflated during feeding;
4) monitor the patient for abdominal distention; and
5) check the tube placement before every feeding (if intermittent) or at least 4 to 8 hours if feedings are continuous (Thelan *et al*., 1998:133).

Enteral feeding may introduce organisms to the stomach if not stored and administered in an aseptic manner (Harris & Miller, 2000:62). The administration of enteral feedings should be performed according to aseptic techniques.

4.4.3. Medical treatment

Under this heading the following will be discussed: antibiotic therapy, the implications of the different methods of prevention of gastric ulcers, positioning of the patient and pain control.

4.4.3.1. Appropriate antimicrobial and medical therapy

In a study performed to evaluate the knowledge and the attitude of critical care nurses it was found that they do not perceive their knowledge in this area as excellent, they are not comfortable with interpretation of laboratory results, or with discussing antibiotic therapy with the physician. Nurses did value their role in the therapy of infections in the intensive care unit (Munro & Grap, 2001:216).

Critical care nurses do not usually prescribe antibiotics, but it is important that they have an understanding of this therapy, as they are involved in the identification for the need, administration and assessment of the effectiveness of this therapy. Critical care nurses should play an important role in the prevention of miss-use of antibiotic therapy and nosocomial infections. Therefore they need a good understanding of pharmacology related to antibiotic therapy.

Prophylactic antibiotics

Prophylactic antibiotic therapy may take different forms, like aerolized, systemic and topic therapy.

Systemic antibiotic therapy is inefficient to prevent ventilator-associated pneumonia (Grap & Munro, 1997:426). According to Young and Ridley (1999:1193), prophylactic therapy can be used only in selective groups like the neutropenic oncology patients. Only two doses of cefuroxime may be administered after intubation in case of secondary head injury and stoke.

In general, broad-spectrum antibiotic use increases the rate of ventilator-associated pneumonia caused by *Pseudomonas aeruginosa* or *Acinetobacter* species (Lynch, 2001:377S; Young & Ridley, 1999:1193). These two organisms are associated with a high mortality rate. However, recently the administration of broad-spectrum parental antibiotics has been promoted in patients with coma but general applications should be studied (Kollef, 1999:632).

The use of aerolized antibiotic therapy has been discontinued, as it has not been proven to be effective in the prevention of ventilator-associated pneumonia and because it led to antibiotic resistant infections.

Selective decontamination of the digestive tract is also not promoted due to its inability to demonstrate effect on mortality, emergence of antibiotic resistance and additional toxicity (Kollef, 1999:632).

Topical application of antibiotic therapy in the oropharyngeal and gastrointestinal tract is widely debated and the major concern is organism resistance (Grap & Munro, 1997:426 and Lynch, 2001:377S).

Empirical Antimicrobial therapy

In the absence of culture results and a condition that requires immediate management, empirical therapy is prescribed. In these cases, a broad-spectrum therapy that covers the most common causative organism is selected. *Staphylococcus aureus* and other gram-negative organisms are usually treated with

"a third generation cephalosporin or a combination of fluroquinolone and an aminoglyside" (Grap & Munro, 1997:425). It is important to have knowledge about the common organisms cultured in the particular intensive care unit or institution, and if an early- or late-onset ventilator-associated pneumonia is present and if patient-specific risk factors are present. Patient factors to be considered include recent gram staining and cultures, severity of the symptoms, recent antibiotic treatment and underlying lung conditions. The patient who receives steroid therapy or has neutropenia should also be considered for antimicrobial therapy (Young & Ridley, 1999:1193).

Prophylactic treatment of patients with neutropenia

Patients with neutropenia are at higher risk for community-acquired and nosocomial infections. In this case prophylactic broad–spectrum antibiotics are administered to patients with neuropenic fever (Kollef, 1999:632).

Correct antimicrobial therapy in the presence of ventilator-associated pneumonia

Correct antimicrobial therapy should include: specificity for the specific causative organism/s and the dosage and timeframe for therapy should be adequate. Inappropriate prescription of antimicrobial drugs worsens the prognosis of the patient. If the therapy is not specific, it may lead to superinfections. However, early appropriate therapy reduces mortality (Young & Ridley, 1999:1193). Therefore, diagnosed ventilator-associated pneumonia should be treated immediately according to culture results. Inadequate dosage may lead to antibiotic resistant organisms.

This emphasizes the need for the presence of a culture result for adequate treatment. The critical care nurse should therefore be able to suspect the presence of a ventilator-associated pneumonia and sample an endotracheal aspirate for microbial sensitivity and culture.

In case of late-onset ventilator-associated pneumonia the organisms are usually antibiotic-resistant pathogens. These organisms are usually associated with a higher mortality one-third due to the infection and two thirds due to the underlying disease. In a patient suspected of having ventilator-associated pneumonia, management should include broad-spectrum antibiotics to cover all possible pathogens (Kollef, 1999:627).

Antimicrobial therapy is not without complications and the critically ill patient is often exposed to antimicrobial therapy. Cefasolin has been associated with a higher incidence of ventilator-associated pneumonia. Patients that received prior antibiotic therapy are prone to the development of ventilator-associated pneumonia caused by *Pseudomonas aeruginosa. A* study indicated that all of the patients who developed a methicillin-resistant *Staphylococcus aureus* were exposed to antibiotics (Grap & Munro, 1997:420).

In the attempt to reverse the increasing rate of antimicrobial resistance, strategies were to restrict the use of antibiotics or to provide guidelines for the management of ventilator-associated pneumonia. Another method is to rotate the antimicrobial agents. The most effective method is to eliminate or reduce antibiotic use as the main goal (Kollef, 1999:632).

Inappropriate and uncontrolled administration of antibiotics is limited in this research with the guidelines for antimicrobial therapy set by the blind investigator.

Monotherapy and combination therapies

Monotherapy may be adequate therapy for ventilator-associated pneumonia, caused by Enterobacteriaceae and more susceptible organisms. Monotherapy may include ciprofloxacin or imipenem (Lynch, 2001:379S).

Combination therapy should only be used to treat multiresistant organisms or pathogens that are likely to be resistant. The aim is to avoid long-term use of empirical combination therapy (Kollef, 1999:632).

The following is a short introduction of the management of ventilator-associated pneumonia. Early identification and management of ventilator-associated pneumonia is essential both for the prognosis for the particular patient and to prevent multi-resistant organisms from contaminating the intensive care unit environment. The American Thoracic Society consensus recommends that severe early-onset ventilator-associated pneumonia should be treated with a monotherapy with β-lactam/β-lactamase inhibitor combination, or a second or third generation cephalosporin. Severe late-onset ventilator-associated pneumonia should be treated with combination therapy with aminoglycoside or ciprofloxacillin and adequate cover for *Pseudomonas aeruginosa* with antipseudomanal β-lactam, such as ceftazidime (Young & Ridley, 1999:1193) as the mortality in this case is very high (Lynch, 2001:378S).

a) Aminoglycosides and β-Lactam

Aminoglycosides are used in combination with β-lactam, as aminoglycosides are ineffective as monotherapy. Another aspect to be considered is that aminoglycosides poorly penetrate lung tissue and therefore the dosage should be optimized for successful treatment. Another combination therapy that is also frequently used is piperacillin/tobramycin and ticarcillin/ tobramycin (Lynch, 2001:378S).

b) Carbapenems

Carbapenems (e.g. imipenem/cilastatin, meronem) has the ability to withstand β-lactamase, but is also used in combination with aminoglycoside in the case of highly resistant organisms (Lynch, 2001:379S).

c) Cephalosporins

Third-generation cephalosporin has been suggested as monotherapy in the treatment community-acquired pneumonia and some hospital-acquired pneumonia. However it is not as effective in the case of severe ventilator-associated pneumonia. The fourth-

generation cephalosporin (cefepime) displays efficacy against gram-positive and gram-negative organisms (Lynch, 2001:379S).

d) β-lactam and fluoroquinolones (ciprofloxacin)

This combination has antipseudomonal activity. However, ciprofloxacin is effective against Enterobacteriaceae as monotherapy. Overzealous use of ciprofloxacin may also lead to resistance and this resistance may even cross-resistant to other antibiotic classes (Lynch, 2001:379S).

e) Piperacillin/Tozabactam

Both drugs are effective against *Pseudomonas aeruginosa* and research has shown it at least as effective as ceftazidime or imipenem/cilastatin (Lynch, 2001:380S).

4.4.3.2. Maintenance of low gastric pH

In the prevention of stress ulcers, histamine$_2$–receptor antagonists are used. These drugs reduce the acidity of the stomach. This therapy reduces the incidence of stress ulcers, but colonization of bacteria can increase. Sucralfate does not increase the gastric pH and bacterial colonization will therefore be reduced (Grap & Munro, 1997:426).

According to Young and Ridley (1999:1191) new pathogens appeared in the gastric content when antacids were used, compared to use of sucralfate. According to these authors, when histamine$_2$–receptor antagonists were compared to the use of sucralfate, histamine$_2$–receptor antagonists showed an increase in ventilator-associated pneumonia rates.

However in a study quoted by Young and Ridley (1999:1191), no significant difference was shown in the development of ventilator-associated pneumonia, ICU stay and mortality in the use of ranitidine and sucralfate. There was a trend of lower ventilator-associated pneumonia in the sucralfate group. Drawing conclusions may

be difficult, but sucralfate may be inadequate for some patients at highest risk of peptic ulceration.

4.4.3.3. Positioning of the patient

The positioning of the patient can be by artificially changed kinetic beds or by the nurse. The ideal position for the patient in the bed is the semi-recumbent position while early mobilization is also important in the prevention of ventilator-associated pneumonia.

Kinetic beds and postural changes

Specialized kinetic beds have been designed to change the patient's position to improve secretion drainage and therefore to prevent ventilator-associated pneumonia, but their efficacy has yet to be proven (Kollef, 1999:631). This type of therapy has the benefit of increasing lung ventilation and improving the drainage of pulmonary secretions of the patient, as the bed rotates on the longitudinal axis to the right and then to the left (Thompson, 1995:699).

Kinetic, or otherwise called continuous lateral rotating therapy (Thompson, 1995:699) is associated with a reduction in ventilator-associated pneumonia, but no difference in the outcome or stay in the ICU was reported in studies. This type of bed is fairly expensive, the data is inconsistent and routine use cannot be recommended for routine use (Ellstrom, 1999:416; Young & Ridley, 1999:1192), but they can be effective in the unconscious and immobile patient.

Semi-recumbent position of the patient

As aspiration is common in healthy adults, the patient receiving mechanical ventilation should be positioned in the semirecumbent position to reduce the occurrence of aspiration (Kollef, 1999:629). Together with frequent position changes, it helps to reduce stasis of secretions (Smulders *et al*., 2002:858).

The supine position is a high risk factor in the cause of ventilator-associated pneumonia, even if the cuff of the endotracheal tube is properly inflated. Gastric content may be aspirated. Suggested measures are to nurse the patient with the head lifted at 45^0 (Grap & Munro, 1997:422; Thomson, 1995:698). In the case of the neurosurgical patient, prescriptions are to nurse the patient at 20^0 or 30^0 (mostly at 20^0) to reduce intracranial pressure and ensure adequate cerebral perfusion. This position does not reach the ideal of nursing the patient in the high fowler's position, but it will limit the time that the patient spends in the supine position. Gastro-esophageal reflux is reduced in the semi-recumbent position, but it is not a total guarantee for the patient who receives mechanical ventilation. The semi-recumbent position does not protect against colonization of the oropharynx. However, it protects against aspiration of gastric content (Orozco-Levi, Torres, Ferrer, Piera, El-Ebiary, De La Bellacasa & Rodrigues-Roisin, 1995:1390).

Early mobilization

Some of the strategies suggested by the Centers for Disease Control and Prevention for the prevention of nosocomial pneumonia are: changing of the patient's position, coughing and deep breathing to reduce atelectasis. The patients that are to receive thoracoabdominal, head and neck surgery are considered to be at higher risk for the development of atelectasis, especially those with pre-existing pulmonary dysfunction. The elderly, obese, malnourished, smokers, are also considered to be at high risk. In the prevention of nosocomial pneumonia early ambulation is advised (Thompson, 1995:699), but can be contra-indicated in the patient who has received head surgery.

After extubation the semi-recumbent position, in the absence of contra-indications, should be the standard management of the patient.

4.4.3.4. Pain control

Pain control in the post-operative period is suggested as one of the measures to prevent nosocomial pneumonia, as pain interferes with deep breathing and coughing (Thompson, 1995:699). Effective pain management of the patient improves removal

of pulmonary secretions and therefore reduces the risk for the development of ventilator-associated pneumonia.

4.5. TRANSGRESSION OF INFECTION-CONTROL STRATEGIES

Strict infection control procedures should be in place by means of policies and procedures. Medical, nursing and ancillary staff should be made aware of the prevention and control programs in place through continuous education. Body fluids and blood should always be considered as potentially infectious and universal precautions should be applied in all circumstances (Williams, *et al.,* 2002:23)

Each month, new products and technology for infection control are available in the market. It is essential that the critical care nurse should be familiar with the manufacturer's directions and receive training where applicable. If not properly applied, infections may occur (University of Michigan, 2002: Online).

4.5.1. Improvement of infection control principles

There is always improvement that can take place regarding infection control measures. The different measures of standard/ universal precautions will be discussed.

4.5.1.1. Standard/universal precautions

The principles of hand decontamination, the use of gloves, masks, gowns and aprons will be discussed below.

Hand decontamination

Hand washing is the best way to prevent ventilator-associated pneumonia, as cross contamination plays a major role in spreading of pathogens. Gram-negative bacteria and *Staphylococcus aureus* colonize on the hands of health care providers. Hand washing reduces cross-colonization and prevents nosocomial pneumonia (Harris & Miller, 2000:63).

Hands should be washed before and after touching the patient and respiratory equipment, or after contact with mucus membranes, respiratory secretions or objects contaminated with respiratory secretions (Harris & Miller, 2000:63).

According to the World Health Organization (Williams *et al.,* 2002:24), the following should be available for hand washing, hand disinfection and surgical scrubbing.

a) Hand washing

The transmission of pathogens via the colonized hands of health-care professionals frequently occurs in the intensive care setting. Procedures like endotracheal suctioning and handling of ventilator circuits increases the risk for cross contamination. Eliminating pathogens from the hands of personnel, aseptic techniques and disinfection of equipment will reduce the risk for cross contamination. In theory, hand washing is sufficient to remove transient organisms from the hands of personnel. Unfortunately, compliance with this basic procedure is poor (Tablan, *et al*., 2003: Online).

Running water, a large washbasin with hands free controls, and anti-splash devices should be available as a standard for hand washing. The products that should be used are antiseptic liquid soap. Materials for the drying of hands should be disposable paper towels, or re-usable sterile single-use paper towels (Williams *et al.,* 2002:24).

b) Hand disinfection

The use of alcohol-based solutions is advised, as it may increase personnel compliance and also reduce the transmission of infections (Tablan, *et al*., 2003: Online). Specific hand disinfectants like 2 to 4% chlorhexadine are recommended for hand washing (Williams *et al.,* 2002:24).

c) Surgical scrub

Training in the current procedure in the preparation for surgical procedures should be provided. Scrubbing of the hands should take place for 3-5 minutes. The

recommended antiseptics are 4% chlorhexidine (Mulder, Small, Botma, Ziady & MacKenzie, 2002:102) or 7.5% povidone iodine (Williams *et al.,* 2002:24).

Gloves

The use of gloves is associated with a decrease in the incidence of infections in the intensive care unit. However, organisms can colonize the gloves and this can lead to outbreaks, which have been traced to personnel who did not change their gloves between patient contacts or procedures. Gloved hands may still be contaminated via leaks in the gloves. It is therefore important that hands should be disinfected after the removal of gloves (Tablan *et al*., 2003 Online).

The use of gloves does not make hand washing obsolete, as the use of gloves is not 100% effective. The same pair of gloves should not be used on different patients and hands should be washed after removal of gloves (Tasota *et al*., 1998: Online). Firstly, gloves should always be worn when they come into contact with blood, body fluids, secretions, excretions, mucus membranes, respiratory secretions and non-intact skin, as a barrier protection. Secondly, gloves should be worn to prevent transmission of organisms from the personnel's skin to mucus membranes and non-intact skin. Thirdly, gloves should be worn to reduce contamination of personnel's hands with microorganisms from the patient or byproducts (Centers for Disease Control and Prevention, 1997: Online).

Masks

Masks should be worn to protect the nose, eyes or mouth of personnel when performing procedures where splashes and spills may take place (Centers for Disease Control and Prevention, 1997: Online). The effectiveness of the surgical mask has always been in doubt and more effective masks with eye protection should be used.

Gowns or plastic aprons

When the literature refers to gowns, it does not refer to a type of cotton overcoats, but to garments that are impermeable to liquids like blood or bloody fluids to protect personnel's clothes and skin (Harris & Miller, 2000:63; Mulder *et al*., 2002:35).

In the prevention of ventilator-associated pneumonia, gowns should be worn in cases where the clothes of the caregiver may be soiled. Gowns should cover all clothing (Mulder *et al*., 2002:35). At the research site, staff are encouraged to rather wear a plastic apron. This protective wear should be taken off when care is provided to another patient (Harris & Miller, 2000:63).

The use of gloves and gowns is not recommended for routine preventative measures, but in case of antibiotic-resistance pathogens, like vancomycin-resistant enterococci (Kollef, 1999:629). Gowns and aprons should not be worn as a general precaution, but only as an infection-control measure. In some cases the gowns and gloves are seldom removed and may even contribute to cross-contamination.

4.5.2. Management of respiratory equipment- related issues

The management of ventilator circuits, pulmonary secretions and heated and heat and moisture exchange humidifiers will be addressed.

4.5.2.1. Ventilator circuits

The principle of the changing of and continuous management of ventilator circuits, are essential in the prevention of ventilator-associated pneumonia. Therefore the changing and the continuous management of ventilator circuits will be discussed.

Changing of ventilator circuits

Ventilator circuits should not be changed more frequently than every 48 hours. The maximum time of tubing left unchanged has yet to be determined (Grap & Munro, 1997:421; Harris & Miller, 2000:63). In a study where research results were compared, the finding was that frequent changes of ventilator circuits do not have any

advantages (Cook *et al.,* 1998:785). Ventilator circuits colonize within 24 hours of their placement. Frequent changes of the circuits do not reduce the colonization. However, ventilator circuits must be replaced when visibly soiled (e.g. pulmonary secretions, vomit or blood) (Kollef, 1999:630).

Fink, Krause, Barret, Schaaff, and Alex (1998:408) did not find a significant difference when ventilator circuits were changed with 7-and 30-day intervals. There is however a reduction in the incidence of ventilator-associated pneumonia from 2-day changes to 7-day changes. This study also utilized heated wire circuits and obviously found a cost saving effect between the 7-and 30-day changing of circuits (Fink *et al*., 1998:411).

Two types of ventilator circuits are available: single use ventilator circuits or multiple ventilator circuits. The latter is usually cleaned with a pasteurization process. This process may fail from time to time, as it does not completely sterilize the ventilator circuit and may therefore contribute to the development of ventilator-associated pneumonia. This is why single use ventilator circuits are used in this research.

When re-usable ventilator equipment is used, policies should outline the process of pasteurization, disinfecting and maintenance of respiratory equipment. In the prevention of introducing organisms to the lower respiratory tract, it is important that there is strict adherence to infection control principles and isolation techniques (Harris & Miller, 2000:63). This also applies to routine changing of the ventilator circuits.

Nurses should protect their hands and also their eyes, clothes and mouth by wearing gloves, protective glasses, plastic aprons and masks during the changing of ventilator circuits (Mathews & Mathews, 2000:19; Quirke & French, 1996:279).

Ventilator circuits will be changed every 7 days in this research. Disposable circuits used in this research do have water traps in the expiration leg of the circuit. Universal

precautions will be addressed in the training of the nursing, and medical staff as well as physiotherapists.

Humidification from sterile water in a vaculiter connected to the reservoir will be used in this research. This will ensure a closed system to prevent contamination of the circuit.

Medication nebulisers should be managed in a sterile manner. When disconnected from the circuit, the nebulizer should be covered in a sterile glove. When any doubt about the sterility of the devise exists, it should be thrown away.

Continuous management of ventilator circuits

The ventilator circuits should be kept free of condensate, as it provides a medium for the growth of bacteria. Draining of the circuits should take place downward away from the patient, to prevent contaminated condensate running down the endotracheal tube (Young & Ridley, 1999:1191). The ventilator circuits should be positioned lower than the patient level to prevent the same consequence. When the patient's position is changed, the same care should be taken to prevent contaminated condensate running down the endotracheal tube. The critical care nurse and other health care providers should take care to prevent inadvertent lavage of the upper airways by condensate from the ventilator circuit (Quirke & French, 1996:279).

When water accumulates in the circuit, it drains into a water trap that can be opened and emptied. These water traps are spring-loaded and when opened the circuit's integrity will not be breached. If condensation takes place, draining of the circuit should take place before the patient is turned. Critical care nurses should wear gloves when water traps are emptied (Quirke & French, 1996:279). The critical care nurse should know that unnecessary manipulation and disconnection of ventilator tubing is detrimental to the patient and should be kept to the minimum (Quirke & French, 1996:279).

Sterile water, rather than distilled water should be used in the reservoirs as Legionella may survive at high temperatures (Quirke & French, 1996:279).

The ventilator tubing should always be correctly positioned and secured by the ventilator arm. The position of the ventilator circuit should be in such a way to prevent back flow of condensate into the patient's airway (Quirke & French, 1996:279).

4.5.2.2. Pulmonary secretions

The nurse is primarily involved with management of secretions and can therefore play an important role in the prevention of ventilator-associated pneumonia via proper hand washing techniques and adhering to sterile suctioning procedures.

Open single-use vs. closed multi-use catheter system

Two types of devices can be used in clearing out pulmonary secretions. The first type is the closed multi-use catheter system, which is a suction catheter covered with a plastic sleeve, preventing hand contamination of the suction catheter. This catheter is connected to the endotracheal tube and the ventilator circuit and remains connected for the period of use. There is an additional port for the administration of the rinsing solutions (Mathews & Mathews, 2000:19).

The use of the closed multi-use catheter system increases the incidence of colonization, but does not increase the incidence of pneumonia, compared to the conventionally used single-use catheter system (open suctioning method) (Harris & Miller, 2000:62). The risk for the development of ventilator-associated pneumonia seems to be the same with both single-use and closed multi-use catheter systems (Kollef, 1999:631). The closed multi-use catheter system provides the benefit of effectively managing pulmonary secretions, without increasing the risk of developing a ventilator-associated pneumonia (Harris & Miller, 2000:62).

The experience of this researcher is that the nursing staff is more likely to remove pulmonary secretions with the closed multi-use catheter system, compared to the open single-use catheter system. The frequency of the suctioning procedure of the closed multi-use catheter system was higher than in the case of the open single-use suction system. The difference can be ascribed to the less time consuming and labour intensity of the first mentioned system. Nursing staff is therefore more likely to suction the patient when necessary and not routinely. The suctioning procedure is more likely performed as the need arises, reducing the risk for the development of ventilator-associated pneumonia.

Opinions concerning the cost involved with both of these systems differ. Direct comparison between the two catheters, will prove that the closed multi-use catheter system is more expensive, but one should calculate all the costs involved with the open single-use catheter system. Cost associated with the use of the single-use catheter system will include the following: time spent in procedure and cost of gloves, masks, caps, sterilization of gauze, sterile work area and suction catheters.

The advantage of the closed multi-use catheter system lies in its lower cost and reduction of contamination of the environment when the patient is suctioned. Daily changes for these catheters are also not necessary (Harris & Miller, 2000:62; Kollef, 1999:631). The use can be extended to 48 hours and even longer, if the device is properly rinsed after every suctioning procedure and if it is not grossly contaminated with secretions. Some centers increase the use of the catheter to 7 days, with no increase in ventilator-associated pneumonia (Mathews & Mathews, 2000:19).

Nurses may minimize the risk of ventilator-associated pneumonia, by using closed-system suctioning devices (also called closed multi-use catheter system), as this suction system prevents breaking of the closed system of the ventilator circuit (Mathews & Mathews 2000:17).

The closed multi-use catheter system provides the patient, in addition to the infection reduction, with the benefit of maintaining positive end-expiratory pressure and fractional inspiratory oxygen at therapeutic levels (Mathews & Mathews, 2000:19).

Physiotherapy

Chest physiotherapy, postural drainage, percussion and vibration, are associated with tracheal suctioning and this has its benefits. However, in some circumstances it may attribute to desaturation. No data exists to prove that the use of physiotherapy prevents ventilator-associated pneumonia (Kollef, 1999:631; Young & Ridley, 1999:1193).

4.5.2.3. Heated humidifiers and heat and moisture exchange humidifiers

Many heat and moisture exchange humidifier filters are available in the market. Heat moisture exchangers have some advantages namely: lower cost (this is controversial as different writers have different opinions regarding cost) and passive operation (do not need heat or electricity), therefore, they are easy to use. In theory, heat and moisture exchangers reduce the incidence of ventilator-associated pneumonia, by reducing the condensate in the ventilator circuits. They should only be considered in patients with no contraindications and not just for their cost effectiveness (Kollef, 1999:631). Manufactures recommend that the heat and moisture exchange humidifiers should be changed daily. This however attributes to increase in cost.

The incidence of pneumonia in the use of heat and moisture exchange humidifiers and heated humidification differ in different studies. In some studies heat and moisture exchange humidifiers showed a reduction in ventilator-associated pneumonia (Bowton 1999:31S). The use of heat and moisture exchange humidifier reduces the cost associated with ventilator circuits. There are other studies that also showed no difference in incidence of ventilator-associated pneumonia in the use of heat and moisture exchange humidifiers and heated humidifiers. The difference in the two studies was the criteria used in the diagnosis of ventilator-associated pneumonia (Bowton, 1999:31S).

When two types of heat and moisture exchange humidifiers were compared, the performance regarding humidification and incidence of ventilator-associated pneumonia, were the same. However the long-term use of these filters should still be researched, as inadequate humidification is still a concern (Thomachot, Vialet, Arnaud, Barberon, Michel-Nguyen & Martin, 1999:926). Another main concern is that the use of heat and moisture exchange humidifiers is associated with more endotracheal tube occlusions, causing asphyxiation and more tenacious secretions (Cook *et al*., 1998:785). This is why heated humidifiers are often used in the long-term ventilated patient.

4.6. CONCLUSIONS

The prevention of ventilator-associated pneumonia is crucial. Standard or universal infection control measures can address the exogenous sources of ventilator-associated pneumonia. Hand washing, barrier protection, appropriate disinfection or sterilization of equipment can address these sources. Education of health care providers, the patient and family is vital.

If one wants to address endogenous sources of ventilator-associated pneumonia, the risk associated with endotracheal and nasogastric tubes should be recognized. Elevation of the head in the prevention of aspiration, aspiration of subglottic secretions, cuff pressure maintenance, providing optimal nutrition, removal of pulmonary secretions, pain control and vaccination are effective measures against the development of ventilator-associated pneumonia (Thompson, 1995: 700).

CHAPTER 5
LITERATURE REVIEW
PREVENTION OF SILENT ASPIRATION

5.1. INTRODUCTION

Silent aspiration is one of the main causes of ventilator-associated pneumonia. Strategies to prevent silent aspiration can be divided into two modalities: removal of subglottic secretions and maintenance of correct endotracheal tube cuff pressure. See Figure 5.1.

In this chapter studies related to both the topic of removal of subglottic secretions, i.e. subglottic suctioning and maintenance of correct endotracheal tube cuff pressure will be discussed.

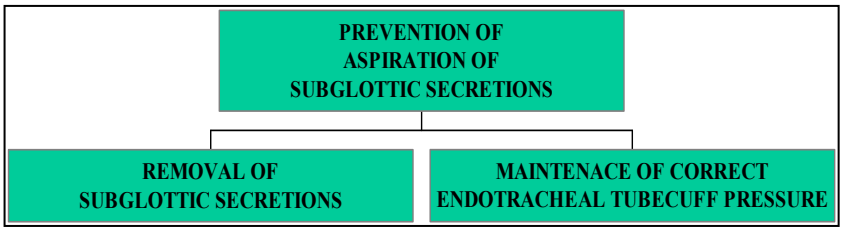

Figure 5.1. Prevention of aspiration of subglottic secretions

5.2. SUBGLOTTIC SUCTIONING

Leaking of contaminated secretions past the cuff of the endotracheal tube, is considered to be one of the most significant risk factors for ventilator-associated pneumonia in the first 8 days of mechanical ventilation (Rello, Sonora, Jubert, Artigas, Rué, & Vallés, 1996:111). Some endotracheal tubes are designed for the removal of subglottic secretions. They have a separate dorsal lumen ending in the subglottic space just above the cuff (See Figure 1.1). The subglottic secretions can be removed by negative pressure. Subglottic suctioning can reduce secretions in this space, but not totally remove fluid from it (Young & Ridley, 1999:1191). This specialized type of

endotracheal tube is not the replacement for an organized approach to infection control measures.

Secretions from the oropharynx accumulate on top of the cuff of the endotracheal tube. The Hi-Lo™ Evac (*Mallinckrodt, St Louis*) endotracheal tube are equipped with an opening on top of the cuff, which allows for the drainage of secretions from this space (Harris & Miller, 2000:57). Removal of these secretions reduces the aspiration of secretions and microorganisms in the lower airway. Research has shown that removal of secretions from this space reduced the incidence of ventilator-associated pneumonia by 50%. Subglottic suctioning reduced colonization of gram-positive bacteria like *H. influenzae,* but the number of *Pseudomonas aeruginosa* or *Enterobacteriaceae* organisms did not decrease. Subglottic suctioning also reduced the time of onset of ventilator-associated pneumonia (Harris & Miller, 2000:57-61). See Figure 5.2.

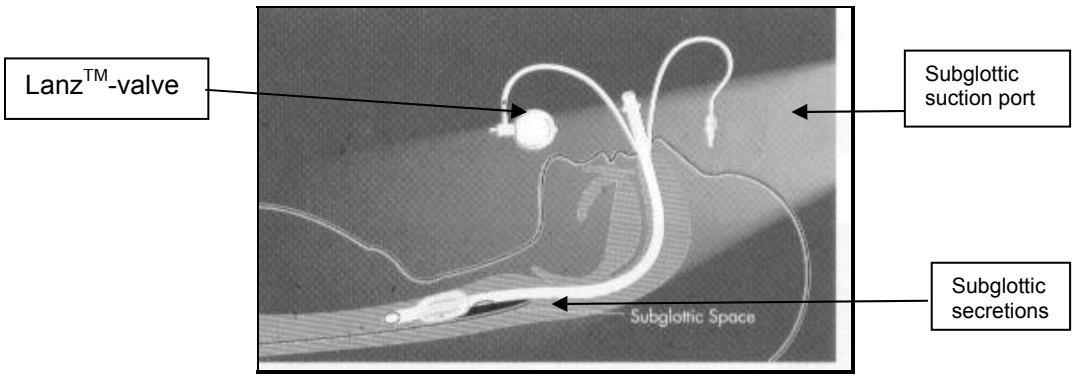

Figure 5.2: Endotracheal tube with subglottic suction function (Mallinckrodt, 2002:2)

Vallés *et al.* (1995:184) found a reduction in the number of gram-positive cocci and *Haemophilus influenzae* organisms and that fewer ventilator-associated pneumonia occurred later in patients who received **continuous aspiration of the subglottic space**. However, no difference was proven in the number of *Pseudomonas aeruginosa* and Enterobacteriaceae organisms.

The problem with this type of tube is that the patient should be initially intubated with this type of endotracheal tube. If intubation with this type of tube has not taken place,

the patient has to be re-intubated. This is not recommended, as re-intubation is associated with the development of ventilator-associated pneumonia (Wunderink, 1999:1156). This will imply that endotracheal tubes with subglottic suction function, should be made available in the emergency services, emergency departments, theatres and wards where the patient is initially intubated.

It is also essential that secretions should be removed from the supra-cuff area before the cuff is deflated before removal or repositioning of the endotracheal tube (Grap & Munro, 1997:426).

5.2.1. Different methods of subglottic suctioning

Literature refers to different methods of removing subglottic secretions. Three of these methods will be discussed. Research still has to determine the ideal method.

5.2.1.1. Aspiration via syringe

One of the methods of the removal of subglottic secretions, is hourly aspiration of secretions with a 10ml syringe. Mahul *et al*. *(*1992:20) used this method originally. The above-mentioned researcher found that the volume of secretions in the subglottic space could be 3.6 ± 2ml in case of endotracheal tubes and 10.5 ± 5ml in case of tracheotomy tubes. He also found that the volume for a 24-hour period ranged up to 100-150ml (Mahul *et al*., 1992:24).

This method was not selected for this research to prevent that staffs' hands get in contact with pathogens. Contact may lead to the colonization of the staffs' hands with pathogens, causing cross-contamination in the research environment.

5.2.1.2. Intermittent aspiration

Another method used to remove subglottic secretions was used in the study of Smulders *et al.* (2002:859). They selected an intermittent method of subglottic suctioning rather than the continuous method. The interval of subglottic suctioning is not clear, but it was performed at a negative pressure of 100mmHg with 20-sec

intervals for duration of 8-sec. Continuous suctioning at a pressure of 100mmHg may lead to tracheal wall damage (Smulders *et al*., 2002:859). The time involved with subglottic secretion removal does not take longer than 10min per day (Mahul *et al*., 1992:24). For the same reason this study has selected intermittent subglottic suctioning.

This method was selected for this research because of the problems associated with methods in 5.2.1.1. and 5.2.1.3. Another reason was considered namely: this is a method that increases the reliability of the research as consistency can be indicated on the *Daily Procedure form.*

5.2.1.3. Continuous aspiration

The manufacturers recommend that continuous aspiration of subglottic secretions are performed at a negative pressure of 20mmHg (Mallinckrodt, 2000:1). The concern is that the continuous suctioning may dry out the tracheal wall, but no indication of this complication was found in these studies.

The reason for not choosing this method is that it will require two suction apparatuses at the bedside, one for continuous subglottic suctioning and one for endotracheal suctioning. Two suction apparatuses are however not available at the research site. The other option is that the same apparatus should be used for both procedures. The adjustment of the suction apparatus may be neglected during the care of the subjects and therefore cause complications of the inner wall of the trachea.

5.3. RESEARCH REGARDING THE PREVENTION OF SILENT ASPIRATION

The following is a summery of the results of research available, related to removal of subglottic secretions. The studies will be presented in the order of the dates of the publications. The results of these studies are compared in Table 5.2.

5.3.1. Prevention of nosocomial pneumonia in intubated patients: respective role of mechanical subglottic secretion drainage and stress ulcer prophylaxis (Mahul *et al*., 1992:20-25)

5.3.1.1. Objective of this study

"To evaluate the prevention of nosocomial pneumonia by limiting tracheal, subglottic and gastric colonization by two different modes: a) subglottic suction and b) prophylaxis of ulcer bleeding" (Mahul *et al*., 1992:20).

5.3.1.2. Results

This study has shown a reduction by half in the incidence of ventilator-associated pneumonia in the case of subglottic suctioning and it also increased the time of onset of the ventilator-associated pneumonia two-fold. Subglottic suctioning had no effect on the subject who already had pneumonia at intubation. This study cultured the same organisms on both sides of the cuff (Mahul *et al*., 1992:24). The method of subglottic suctioning was the method selected for this particular study.

5.3.1.3. Conclusions

This is one of the first studies that indicated the value of subglottic suctioning. It indicated a reduction of 50% in the incidence of ventilator-associated pneumonia. The study also indicated that the leaking of subglottic secretions past the cuff causes ventilator-associated pneumonia. The organisms cultured above the cuff and the causative organisms were the same (Mahul *et al*., 1992:24).

5.3.2. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia (Vallès *et al*., 1995:179-185)

5.3.2.1. Objective

"To determine whether continuous subglottic suctioning prevents nosocomial pneumonia in mechanically ventilated patients" (Vallés *et al*., 1995:179).

5.3.2.2. Results

Continuous subglottic suctioning reduced ventilator-associated pneumonia by 43.4%. There was a significant reduction in pneumonia within the first days of ventilation with this simple, inexpensive procedure. In this research there was no difference found after the first week of ventilation. The onset of *Pseudomonas aeruginosa* ventilator-associated pneumonia was not prevented but delayed in patients that received continuous subglottic suctioning. The highest mortality was also in the control group. There was also a reduction in the use of antibiotics in the continuous subglottic suctioning group and therefore cost saving resulted. The researchers emphasized maintaining correct cuff pressure management (Vallés *et al*., 1995:179-185).

5.3.2.3. Conclusion

Again a good result in the prevention of ventilator-associated pneumonia was indicated. This research indicates the importance of initial intubation of the patient with this type of endotracheal tube. The result indicated a reduction in the main problems associated with ventilator-associated pneumonia: high mortality, morbidity and medical cost. The maintenance of cuff pressure is important to prevent aspiration of secretions past the endotracheal cuff.

5.3.3. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac patients (Kollef *et al.,* 1999:1339-1346)

5.3.3.1. Objective

"To determine whether the application of continuous aspiration of subglottic secretions is associated with a decreased incidence of ventilator-associated pneumonia" (Kollef *et al*., 1999:1339). The population group was patients that underwent cardiac surgery.

5.3.3.2. Results

Their findings were that continuous subglottic suctioning could be safely applied in patients undergoing cardiac surgery. Ventilator-associated pneumonia was

significantly delayed among patients undergoing cardiac surgery by using this simple-to-apply technique. There was no significant difference in the duration of ventilation, lobar atelectasis, length of stay in the intensive care unit and hospital and hospital mortality in the group that received continuous subglottic suctioning (Kollef *et al*., 1999:1339).

5.3.3.3. Conclusion

Subglottic suctioning did not reduce the time of ventilation, but it increased the onset of ventilator-associated pneumonia, when long-term ventilation was required. Again, no complications of subglottic suctioning where identified. This is one of the only studies I could find, which implemented this technique in a high risk group of subjects.

5.3.4. A randomized clinical trial of intermittent subglottic suction drainage in patients receiving mechanical ventilation (Smulders *et al.,* 2002:858-862)

5.3.4.1. Objective

"To study the effect of subglottic secretion drainage on the incidence of ventilator-associated pneumonia in patients receiving mechanical ventilation" (Smulders *et al.,* 2002:858).

5.3.4.2. Results

Patients that received subglottic suctioning had a statistically lower incidence of ventilator-associated pneumonia than those intubated with the conventional tube of 15.6 episodes per 100 ventilator days (Smulders *et al*., 2002:861). These researchers did not find any statistical difference between the length of stay in the intensive care unit, length of stay in the hospital, duration of mechanical ventilation and mortality between the control and the group that received subglottic aspiration. This result may be because of the small size of the study.

It was found that there was an increase in mortality if Pseudomonas and Acinetobacter species are involved (Smulders *et al*., 2002:861). In this study, 58%

Pseudomonas aeruginosa and *Klebsiella pneumoniae* were cultured in the subglottic secretions and these subjects developed ventilator-associated pneumonia. In 33% of the subjects *Staphylococcus aureus* was cultured (Smulders *et al*., 2002:861).

Clinical criteria were used for the diagnosis of ventilator-associated pneumonia rather than obtaining aspirations with a bronchoscope. This, however, is acceptable to some writers (Smulders *et al*., 2002:862).

The sample size was considered to be a limitation, because 28% of the subjects were ventilated for less than 72 hours. The final conclusion was that subglottic suctioning should be applied routinely, when patients are ventilated for more than 72 hours (Smulders *et al*., 2002:861).

5.3.4.3. Conclusion

Subglottic suctioning reduced the incidence of ventilator-associated pneumonia. However, *P aeruginosa*, *K Pneumoniae* and *S aureus* remained prevalent. The processes related to these organisms may be different than those related to aspiration past the endotracheal cuff.

Table 5.1: Comparison of subglottic suctioning research findings

Results of study group	Mahul *et al*. 1992	Valles *et al.* 1995	Kollef *et al*. 1999	Smulders *et al*. 2002
Hourly subglottic suctioning	✔			✔
Continuous subglottic suctioning		✔	✔	
Incidence of ventilator-associated pneumonia	Reduced with 50%	Reduced gram positive and *H. influenzae* organisms	Fewer *S. aureus* and *H. influenzae*	Statistically significant reduction (p value < 0.001)
Difference in outcomes	Not measured	-	-	-
Onset of	Prolonged	Prolonged *P*	Prolonged	Prolonged the

ventilator-associated pneumonia	onset (two fold) and colonization	*aeruginosa* onset	onset (2.7 days)	onset
Emphasize	Intermittent subglottic suctioning reduced the incidence of ventilator-associated pneumonia	Continuous subglottic suctioning reduced incidence of ventilator-associated pneumonia	Simple safe method in prevention of ventilator-associated pneumonia	Intermittent subglottic suctioning reduced the incidence of ventilator-associated pneumonia

5.4. ADDITIONAL STUDIES ON SUBGLOTTIC SUCTIONING

Two additional studies related to subglottic suctioning will be discussed under this heading.

5.4.1. Pneumonia in intubated patients: role of respiratory airway care (Rello *et al.*, 1996:11-115).

5.4.1.1. Objective

"To evaluate potential risk factors for pneumonia within the first 8 days of mechanical ventilation in intubated patients receiving continuous subglottic suctioning." (Rello *et al*., 1996:111).

5.4.1.2. Results

In this study it was found that the volume of subglottic secretions aspirated decrease 2 days before the development of pneumonia. It was also found that a low persistent cuff pressure of less than 20 cmH_2O is a risk factor for the development of ventilator-associated pneumonia (Rello *et al*., 1996:113)

This research indicated risk factors like the presence of coma, and continuous sedation. Antibiotics had a protective effect. They also list the following additional risk factors: chronic obstructive pulmonary disease, antecedent cardiopathy, cirrhosis, diabetes, steroid therapy, muscle relaxants used, failure of continuous subglottic suctioning, multiple changes of endotracheal tube and cardiopulmonary resuscitation (Rello *et al*., 1996:113).

This study emphasizes two aspects: maintenance of adequate cuff pressure and continuous subglottic suctioning. Both these procedures do not have a "down side", as in the case of prophylactic antibiotics and selective decontamination of the digestive tract (Rello *et al*., 1996:114).

5.4.1.3. Conclusion

The reduction of subglottic secretions before the development of ventilator-associated pneumonia may indicate that secretions started leaking past the cuff. The cuff pressure of less than 20 cmH_2O leads to secretions leaking past the cuff and is therefore associated with ventilator-associated pneumonia.

5.4.2. Continuous subglottic suctioning for the prevention of ventilator-associated pneumonia (Shorr & O'Malley, 2001:228-235)

5.4.2.1. Objective

This study's focus was "to compare the cost related to continuous subglottic suction endotracheal tubes and the standard endotracheal tube to the cost when ventilator-associated pneumonia develops" (Shorr & O'Malley, 2001:228).

5.4.2.2. Results

In this study's population were subjects who required "nonelective intubation". The cost calculated in this study was compiled with the cost of: 1) diagnosis of ventilator-associated pneumonia, 2) its treatment and 3) the degree to which it prolongs intensive care (Shorr *et al*. 2001:229).

In the study of Shorr & O'Malley (2001:232), the cost effect was calculated for different scenarios and the cost saving ranged from $1,936 to $7,799. In their conclusion they remarked that endotracheal tubes with continuous subglottic suctioning capabilities are highly cost-effective and should regularly be employed in nonelective endotracheal intubations. Even though the cost of the continuous

subglottic suctioning endotracheal tubes is higher than the conventional tubes, the high cost associated with ventilator-associated pneumonia outweighs it (Shorr & O'Malley, 2001:232).

5.4.2.3. Conclusion

Again the saving result of this technique, due to the prevention of ventilator-associated pneumonia, has been demonstrated in this research.

5.4. MAINTENANCE OF CORRECT ENDOTRACHEAL TUBE CUFF PRESSURE

The management of cuff pressure includes two considerations: ensure enough pressure to prevent secretions leaking past the cuff and pressure that allows for sufficient perfusion of the tracheal wall. Literature does not indicate a single best method of cuff inflation. In fact, research recommendations are inconsistent and conflicting (Crimlisk, Horn, Wilson, & Marino, 1996:225).

An outdated practice was to deflate cuffs to decrease cuff pressure on the tracheal wall. This however is not practiced presently, due to an increased risk for aspiration and hypoxia. (Crimlisk *et al*., 1996:226).

The first type of cuff was the low-volume, high-pressure type of cuff, followed by the high-volume low-pressure type of cuff. The newer type of cuff has a thinner wall and a smaller diameter. The ideal type of endotracheal tube should be able to inflate during inspiration and partially deflate during expiration to prevent tracheal ischemia (Crimlisk *et al*., 1996:232). The trachea dilates during inspiration and higher cuff pressure is required during inspiration to ensure a seal. This phenomenon is call "chasing the trachea". As the pressure is applied the trachea looses its integrity over

time. Increased amounts of air are required to ensure sealing. More pressure is applied and constant dilatation results (Crimlisk *et al.,* 1996:232).

5.5.1. Methods to inflate endotracheal tube cuffs

Two methods of cuff inflation are described in literature, namely: the minimal leak technique and minimal occlusive volume. Research has not established the ideal method for inflation of the cuff yet. In South Africa the critical care nurse is responsible for the inflation and the monitoring of these pressures compared to the respiratory therapists in the United States.

5.5.1.1. Minimal occlusion volume

The minimal occlusion volume is the smallest volume of air in the cuff that prevents air leaking on inspiration. This is the method of choice as it ensures ventilator volume delivered (Crimlisk *et al.*, 1996:226).

This method stabilizes the endotracheal tube during movement and decreases the incidence of aspiration. (Research has established that it does not totally prevent aspiration.) This method is ideal for the patient who moves frequently, or those who experience changes in lung compliance. The problem with this method is that it may provide pressure beyond what is required (Crimlisk *et al.*, 1996:226). This will therefore lead to tracheal wall ischemia.

5.5.1.2. Minimal leak technique

The minimal leak technique is the smallest volume of air in the cuff that allows for a small air leak on inspiration (Crimlisk *et al*., 1996:225).

This technique has been designed to protect the tracheal wall against trauma caused by the cuff by minimizing the cuff-to-tracheal wall pressure. The problems with this method of inflation are that it does not ensure volume ventilation, it could potentially dry out the tracheal wall and aspiration of subglottic secretions (Crimlisk, *et al*., 1996:226).

5.5.2. Maintaining correct cuff pressure

Firstly, cuff pressure should be adequate to prevent secretions from leaking past the cuff to the lower respiratory airways (Kollef, 1999:630). Secondly, cuff pressure should be maintained below tracheal capillary perfusion pressure, which is between 20-30mmHg. Tracheal blood flow is impaired at 22mmHg (30cmH_2O) and totally occluded at a pressure of 37mmHg (50cmH_2O). Some authors recommend that cuff pressures should not exceed 18mmHg (25cmH_2O) to prevent tracheal injury. Others again state that cuff pressure should not be lower than 18mmHg, due to the risk of aspiration. This again is not a guarantee, as tracheal rupture and dilatation has been recorded when cuff pressures were kept below 22mmHg (Crimlisk *et al.*, 1996:226).

5.5.3. Cuff pressure measurement

Sphygmomanometers, special aneriod cuff manometers and electronic cuff pressure devices can be used to measure cuff pressures. The frequency of cuff pressure monitoring ranges from continuously 8-hourly, up to daily (Crimlisk *et al.*, 1996:226). The frequency of 8-hourly may be insufficient in the haemodynamically unstable patient.

Over-inflation of the cuff should also be avoided as to prevented ischemic complications of tracheal wall. A local research determined that if a bag with 50 or 100ml 0,9% Sodium chloride with administration set, is connected to the pilot port of the cuff valve, and elevated 30 cmH_2O above the patient, a constant pressure of 30 cmH_2O is applied (Moll, de Villiers, Claassen & Joubert, 2003:10). If cuff pressures increase due to laryngeal spasm or edema, air is displaced into the bag and the opposite occurs in case of a decrease in pressure. This is a good alternative method to maintain correct cuff pressure.

5.5.4. Types of endotracheal tube cuffs

One of the leading causes of ventilator-associated pneumonia is subclinical leaking of subglottic secretions past tracheal cuffs (Young, Basson, Hamilton, & Ridley, 1999:559).

Three types of endotracheal tubes are available to address these problems: high-volume low-pressure cuffs (e.g. HiLo™ Evac (***Mallincrodt Athlone, Ireland***)), low-volume high-pressure cuffs and pressure-limited cuffs.

5.5.4.1. Low-volume, high-pressure cuffs

Low-volume, high-pressure cuffs are associated with tracheal wall damage and cannot be used for long-term ventilation (Young & Ridley, 1999:1191).

5.5.4.2. High-volume, low-pressure cuffs

High-volume, low-pressure cuffs do not totally prevent aspiration from the subglottic space (Young & Ridley, 1999:1191). The incidences of aspiration in patients with high-volume, low-pressure cuffs are from 20% to 40% (Mahul *et al*., 1992:23).

5.5.4.3. Pressure-limited cuff

A new design of tracheal tube cuff, the pressure-limited cuff is a low-volume, high-pressure cuff, which only applies a pressure up to 30 cmH_2O, providing protection against aspiration to the lungs. The aspiration rate is reduced to 87% with the high-volume, low-pressure cuff and in the pressure-limited cuff it was 0%. Positive end expiratory tidal volume pressure and lubrication of the cuff, temporarily prevent cuff leaks in high-volume, low-pressure cuffs (Young & Ridley, 1999:1192). This type of cuff is considered as the bench-top model as it does not have the folds that the high-volume, low-pressure has and therefore prevents leakage past the cuff (Young *et al*., 1999:559).

5.5.4.4. Lanz™ valve

The Lanz™ valve is a pressure-regulating device that connects to the pilot balloon of the cuff. In circumstances where long-term intubation is expected, endotracheal tubes specifically designed with the Lanz™ valve can be utilized. See Figure 5.3.

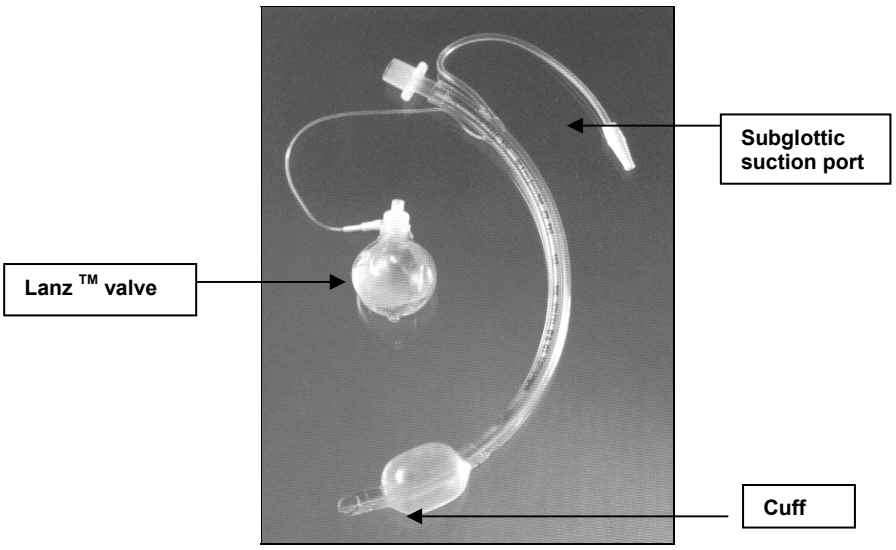

Figure 5.3: Example of HiLo™ Evac Lanz endotracheal tube (M*allincrodt* A*thlone,lireland)* (Mallinckrodt, 2002:2)

The Lanz ™ valve is inflated with 40 cc of air and will maintain the cuff pressure from 25 to 33 cm H_2O. The Lanz ™ pressure-regulating valve automatically regulates pressure by expansion and contraction of the balloon (Mallinckrodt Medical, 2000). Clinical trials regarding this type of device could not be found.

5.6. RESEARCH REGARDING MAINTENANCE OF ADEQUATE ENDOTRACHEAL TUBE CUFF PRESSURE

Below is a discussion about researches related to cuff pressure management.

5.6.1. Aspiration beyond endotracheal cuffs (Seegobin & van Hasselt, 1986:279-279).

5.6.1.1. Objectives

To compare the incidence of aspiration of dye past a variety of large volume cuffed tubes and red rubber low-volume cuffs inflated to clinically seal in a group of 30 patients (Seegobin & van Hasselt, 1986:273).

5.6.1.2. Results

Early studies indicated the concern with mucosal injury to the trachea and aspiration past the cuff. The conclusion of this research was that in the high-volume, low-pressure and the low-volume high-pressure cuff types, leaking past the cuff was detected. High-volume, low-pressure cuffs were designed to reduce tracheal wall damage due to limited blood flow to the area of the inflated cuff, but did not guarantee prevention of cuff leaks at a cuff pressure of 25 cm H_2O (Seegobin & van Hasselt, 1986:273). Even when the intracuff pressure was inflated to 50 cmH_2O, leaking past the cuff was detected (Seegobin & van Hasselt, 1986:275). Conclusions were that cuff pressures greater than 30 cmH_2O reduce tracheal mucosal blood flow and that pressures between 40-50 cmH_2O obstructed blood flow (Seegobin & van Hasselt, 1986:276). They also concluded that even if the patient is breathing spontaneously, the potential for aspiration is greater (Seegobin & van Hasselt, 1986:278).

5.6.1.3. Conclusion

Even though the high-volume, low-pressure type of endotracheal tube cuff is an improvement on the low-volume, high-pressure, there is still aspiration past the cuff that takes place. To prevent this leaking past the cuff, it is essential to inflate the cuff to pressures that will cause reduced blood flow to the tracheal wall.

5.6.2. Artificial airways: A survey of cuff management practices (Crimlisk *et al.,* 1996:225-235)

5.6.2.1. Objective

To determine current endotracheal and tracheostomy tube cuff practices in adult and pediatric populations, and to compare current adult cuff management practices with those reported in use in 1984 and 1987" (Crimlisk *et al.,* 1996:225).

5.6.2.2. Results

In the development of endotracheal tube cuffs the evolution was from low-volume, high-pressure cuffs to high-volume, low-pressure designs. The present third

generation cuff designs offer a thinner cuff wall and smaller diameter (Crimlisk *et al*., 1996:225).

A misconception about the trachea is that it acts like a pipe. In contrast, the trachea is a dynamic organ that changes in size during inspiration and expiration. The ideal cuff may be a cuff that inflates during inspiration and partially deflates during expiration (Crimlisk *et al*., 1996:225).

Results in this study will be discussed. Firstly, the frequency of monitoring cuff volume ranged between every 8 to 24 hours. The nurse became more and more responsible to monitor cuff pressures than previously. Secondly, implications for clinical practice are that standards have to be set for cuff pressure management. Thirdly, the minimal occlusive volume technique has been selected as the standard for cuff inflation. Cuff pressure should be maintained to ensure capillary perfusion between 20 to 30mmHg. Fourthly, routine deflation of cuffs should be discouraged (Crimlisk *et al*., 1996:226).

5.6.2.3. Conclusion

This early research indicated the importance of cuff pressure measurement to reduce the complications of the endotracheal tube cuff.

5.6.3. Influence of airway pressure on minimum occlusive endotracheal tube cuff pressure (Guyton, Barlow & Besselievre, 1997:91-94)

5.6.3.1. Objective

To examine the *in vivo* relationship between peak inflation pressure and the minimum occlusive pressure of a high-volume, low-pressure endotracheal tube cuff that may in some circumstances promote tracheal complications" (Guyton *et al*., 1997:91).

5.6.3.2. Results

As the peak airway pressure increases, the minimum occlusive pressure (the minimum pressure required to ensure leakage of air past the cuff) has to be increased. Thus, the patient supported by high peak pressure ventilation is at higher risk of developing tracheal ischemic complications, even if the high-volume, low-pressure endotracheal tube is used (Guyton *et al.,* 1997:93).

5.6.3.3. Conclusion

An increase in peak airway will eventually lead to air leaks past the cuff. Some nurses may be inclined to increase cuff pressure causing ischemic complications. Ventilating a patient with high peak airway pressures, may even cause secretions to leak past the cuff. Therefore high peak pressures may be associated with the development of ventilator-associated pneumonia. In these cases, it should be standard practice to perform subglottic suctioning, as secretions may leak past the cuff. Increasing the cuff pressures will lead to ischemic damage of the trachea.

5.6.4. Leakage of fluid around low-pressure tracheal tube cuffs

(Oikkonen & Aromaa, 1997:567-569)

5.6.4.1. Objective

"The aim of the study was to evaluate leakage of liquid past the low-pressure cuffs of tracheal tubes" (Oikkonen & Aromaa, 1997:567). Ten different types of tracheal tubes were tested in a PVC mock trachea at different intra-cuff pressures, for leakage of fluids. (The Hi-Contour™, and HiLo™ tracheal tubes of *Mallinckrodt Medical, Athlone, Ireland*, were included in this study.)

5.6.4.2. Results

The best tube that appeared to be leak proof was the HiLo™ (***Mallinckrodt Medical, Athlone, Ireland****)* (more than 5 ml in 5 minutes) at a pressure of 40cmH_2O. The second best tube, the Hi-Contour™ (***Mallinckrodt Athlone, Ireland****)* was leak proof at a pressure of 50cm H_2O. The rest of the tubes leaked profusely (less than 20ml in 5 minutes) even at a pressure of 50cmH_2O. The researcher emphasized the fact that

the patient may aspirate during anaesthesia, as the duration of any surgical procedures is longer than 5 minutes (Oikkonen & Aromaa, 1997:568).

Intra-cuff pressure should be lower than 30cmH_2O to allow for capillary perfusion and therefore will not sufficiently protect against aspiration. "An ideal cuff design awaits development" (Oikkonen & Aromaa, 1997:568).

5.6.4.3. Conclusion

The type of endotracheal tube that provided the least leaking past the cuff, was the Hi-Contour™ (***Mallinckrodt Athlone, Ireland).*** This type of tube was the tube for the control group. This research also indicates the importance of cuff pressure measurement during the surgical procedure and was part of the Standard Operating Procedure (see Addendum 1).

5.6.5. Prevention of tracheal aspiration using the pressure-limited tracheal tube cuff (Young *et al*., 1999:559-563)

5.6.5.1. Objectives

"To compare the pressure-limited cuff with its inflation device and a high-volume, low-pressure cuffed tracheal tube, with intermittent pressure checks, for leakage of dye past the cuff into the trachea in the mechanically ventilated critically ill patient" (Young *et al.,* 1999:559).

5.6.5.2. Results

A new design of cuff, the pressure-limited cuff, was compared with the high-volume, low-pressure type cuff and the low-volume, high-pressure endotracheal tube, regarding the leakage of subglottic secretions past the endotracheal tube. The high-volume, low-pressure cuff forms longitudinal folds, allowing for leaking of the subglottic secretions. The pressure-limited cuff however does not have these folds. The advantage that the pressure-limited cuff has over the low-volume, high-pressure type of cuff is that the first mentioned protects against excessive pressure on the

tracheal wall. This study was performed by comparing the leakage of dye injected on top of the different types of cuffs (Young *et al*., 1999:559-560).

None of the patients intubated with the pressure-limited cuff, had leakage leaked past the cuff, but 3 of the subjects intubated with the high-volume, low-pressure cuff, initially had leakage past the cuff and as the time of ventilation increased, some of the other subjects also had leakage past the cuff (Young *et al*., 1999:562). This study however did not assess the occurrence of ventilator-associated pneumonia.

5.6.5.3. Conclusion

Although the high-volume, low-pressure type of cuff is more leak proof than the conventional type of tubes, the pressure-limited cuff is an improvement. If studies in the future indicate that these types of cuff prevent leaking of subglottic secretions, subglottic suctioning will then not be necessary.

Table 5.2: Summery of studies related to cuff pressures

	Seegobin & van Hasselt, 1986	Crimlisk *et al.,* 1996	Guyton *et al*., 1997	Oikkonen & Aromaa, 1997
Technique of cuff inflation		Minimal occlusion volume	Minimum occlusion volume technique not recommended	
Recommended cuff pressure		Below 20-30 mmHg (27-40cmH_2O)	25mmHg (> 34 cmH_2O)	40-54mmHg (30-40cmH_2O)
High volume, low pressure cuffs	✔		✔	✔
Maximum occlusion pressure 30cm H_2O	✔			
Low volume cuffs, high pressure cuffs	✔			
Maximum occlusion pressure 40 –50cm H_2O	✕			
Discourage cuff deflation techniques		✔		✔

5.7. CONCLUSIONS

Removal of subglottic secretions is one of the most effective interventions in the prevention of ventilator-associated pneumonia. Continuous subglottic secretion aspiration requires a specialized type of endotracheal tube, but the time involved is limited to about 10 minutes per 24 hours. The critical care nurse can easily perform this procedure. Adverse effects of subglottic suctioning have not been identified and it can therefore be performed without any complications.

Management often does not adhere to evidence-based recommendations on correct cuff inflation, which is essential to prevent over-inflation complications and leakage past the cuff. Measuring of cuff pressure is a practice that will take only seconds to perform, but complications due to incorrect pressure, will result in increased morbidity, mortality and high medical cost.

CHAPTER 6

RESEARCH METHODOLOGY

6.1. INTRODUCTION

This chapter describes the research methodology, which has been followed to determine the effect of three types of endotracheal tubes on ventilator-associated pneumonia.

6.2. AIM OF THE STUDY

The aim of this study was to determine the effect of three types of endotracheal tubes on ventilator-associated pneumonia.

6.3. OBJECTIVES

The research objectives were to compare three groups of subjects, intubated with different types of endotracheal tubes, regarding the:

a) incidence of ventilator-associated pneumonia;
b) risk factors;
c) causative organisms;
d) length of stay in intensive care;
e) cuff pressures;
f) morbidity; and
g) mortality.

6.4. RESEARCH DESIGN

The research design, population, sample, subject identification, as well as screening of subjects, will be discussed.

A single center, blind, prospective, controlled clinical trial was selected to investigate

the effect of three types of endotracheal tubes on ventilator-associated pneumonia. See Figure 6.1. for the Flow Diagram of **sampling process** and Figure 6.2 for the Flow Diagram of the **implementation of the research**.

6.4.1. Single center

The research site is the setting at which the research is conducted. The setting of the research makes the study more meaningful, and can therefore be generalized (Uys & Basson, 2000:42-43). In this study, the setting was a tertiary hospital providing care to patients requiring advanced medical care. The patients admitted to tertiary hospitals have many risk factors like, age, chronic diseases, compromised immune system etc. Consequently, this study is quite meaningful, due to the risk factors involved with this population.

The advantages and disadvantages of a single-center site are listed in Table 6.1. The advantages and disadvantages where interpreted as the opposite of a multi-center trial as listed by Spilker (1991:284).

Table 6.1: Advantages and disadvantages of a single-center site

Advantages

1. Administrative arrangements and management are simpler.
2. Cost is less, compared to multi-center sites.
3. Only one Ethics Committee is involved.
4. Investigator gets more recognition through the publication(s) of results.

Disadvantages

1. Slower patient recruitment.
2. Complex protocols cannot be implemented due to limited resources.
3. More opportunity for one person to be bias.
4. Data processing and analysis to be conducted at a lower level.
5. Heterogeneous patient population may be threatened.

(Spilker, 1991:284).

One of the disadvantages experienced in this study was the slow recruitment of subjects. The small sample size will be discussed later under 6.18.1.

A single center site was selected due to the different variables involved when selecting different research sites. More reasons for not selecting a multi-center site were the limited accessibility in the private sector to nursing records, laboratory results and chest X-rays (as the private sector was the only other option). Ensuring adherence to the research design at different research sites would also be a challenge, as only one researcher was involved in this study. Differences in the nursing and medical management of subjects, between the public and private sector, may introduce another variable to the study and were therefore avoided.

In the private sector, the nursing management of neurosurgical patients is performed by different categories of nurses. At the research site, only registered nurses were assigned to care for the neurosurgical patients in the intensive care unit.

6.4.2. Blind study

Blindness means the researcher and/or subjects are not aware of the assigned study group. If the researcher is aware of the assignment, it may influence the outcome (Joubert, Bam & Cronje, 1999:24). In this study the researcher knew to which study group the subject was assigned. The subjects were not aware of the assignment. The researcher, however, did not make the diagnosis of ventilator-associated pneumonia, but a blind investigator was used for this purpose.

The blind investigator (see qualifications 6.8.3) did not have any access to the subjects and was also not aware of the type of endotracheal tube used in the particular subject. It was not possible to identify the type of endotracheal tube on chest X-ray. The use of a blind investigator reduces bias in the research (ICH Guidelines, 2002:3; Spilker, 1991:15). Blindness must be used even if objective measures such as laboratory equipment are used, as knowledge of the group may influence the researcher's or subject's acts (Joubert *el al*., 1999:24).

6.4.3. Controlled clinical trial

A clinical trial is an investigation to discover or verify the clinical effects, adverse or effects, absorption, distribution, metabolism and excretion (in case of pharmacological products) (ICH Guidelines, 2002:3). According to Burns and Grove (1997:279), clinical trials have not been used until recently in nursing research. The purpose of clinical trials in nursing is to examine nursing practice or to test theory-based nursing practice. The latter was the purpose in this research.

The main differences between descriptive and experimental studies, are that descriptive studies describe the existing situation and the experimental studies manipulate the situation (Clark & Hockey, 1989:19).

Clinical trials use large numbers of subjects to study the effects of a treatment (subglottic suctioning in this study) on those who did not receive the treatment (control group). The treatment must be equal and consistently applied and outcomes must be measured consistently. Coordination of this kind of study requires much time and effort. The cost involved in clinical trials is much higher (Burns and Grove, 1997:279-280). The abovementioned statements are very true, but the value of this type of study is underestimated and is therefore worth the effort.

6.5. POPULATION AND SAMPLE

The population is all the members or units of some clearly defined group of people, objects or events that is to be studied (Uys & Basson, 1995:86). The sample on the other hand is the number of elements of the population being studied. Sampling is the process by which the sample is drawn from the population (Uys & Basson, 1995:87). The population, the sample and the sampling process will now be discussed. See figure 6.1. for the Flow Diagram of the sampling process of the study.

6.5.1. Population

According to Burns and Grove (1997:293), the definition of a population is the entire set of individuals or elements that meet the sample criteria and which the researcher

has reasonable access to. Sample criteria are the characteristics that a prospective candidate should have to be part of the target population (Burns & Grove, 1997:293). The sample criteria in this study were selected to ensure homogeneity of the study group. Sample criteria should not be so narrow as to limit the sample size (Burns & Grove, 1997:293).

The population selected was comprised of candidates who were admitted to the Neurosurgical Intensive Care Unit of a public tertiary hospital in Bloemfontein; were intubated in theatre before neurosurgery or required intubation in the Neurosurgical Intensive Care Unit and met the criteria of the study.

This population group of neurosurgical patients was selected, as they are a high risk group for the development of ventilator-associated pneumonia (see Chapter 3). Subglottic suctioning and cuff pressure management have been previously studied in general population groups, except for a study in cardiac surgery subjects (Kollef *et al*., 1999:1339-1346). The problem of the previously mentioned study is that cardiac surgery patients are usually extubated after 24-48 hours and complications of long-term ventilation were not studied.

6.5.2. Sample

The sampling in a study is the selection of a group of people, events or behaviours for study purposes. The purpose of sampling is to select a sample that will reflect the population (Burns & Grove, 1997:293). The sampling process and sampling method will now be discussed.

6.5.2.1. Sampling method

The sampling method of this study was a convenience sample of all candidates admitted to the Neurosurgical Ward or Neurosurgical Intensive Care Unit of a tertiary hospital in Bloemfontein. This group of subjects was selected on accessibility, to maintain the homogeneity of the group and to control extraneous variables.

A convenience sampling forms part of non-probability sampling methods, as not every candidate has an opportunity to be included in the sample. The danger with non-probable sampling, is the sample may not be representative. However, this type of sampling is commonly used in nursing research (Burns & Grove, 1997:302). Convenience sampling opens the doors to bias in a study. Subjects are included just because they happen to be at the right place at the right time. In this case, subjects are enrolled into a study until the desired number of subjects has been reached. The benefit of convenience sampling is that it requires less time to acquire than probability sampling. Convenience sampling is useful in exploratory studies, but is not acceptable for confirmatory studies (Burns & Grove, 1997:302-303).

6.5.2.2. Sampling process

In this research a candidate was considered as a person who was a prospective candidate who had not jet given consent to be enrolled. A subject is therefore a candidate that has given consent to be enrolled into the research. The sampling process is demonstrated in Figure 6.1 below and the explanation will follow the figure.

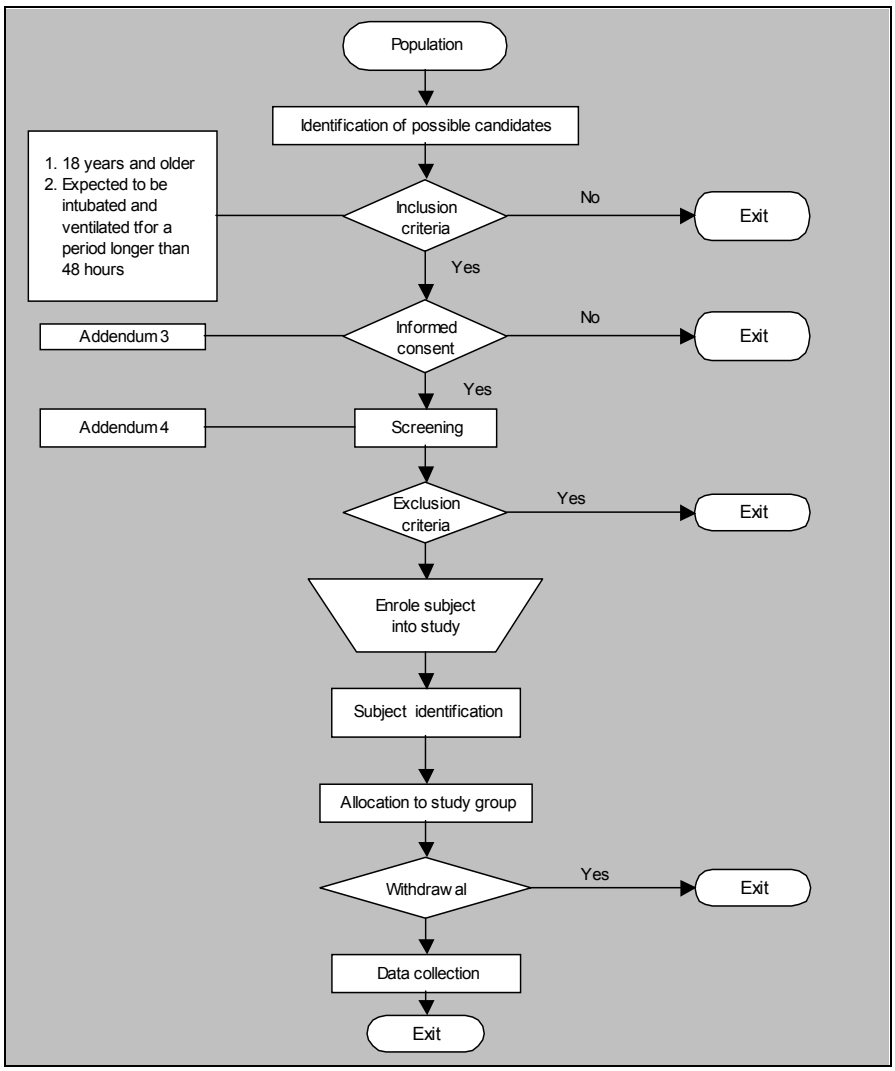

Figure 6.1: Flow diagram of sampling process

Identification of possible candidates

In the initial planning of the study, the neurosurgeon should have notified the researcher of prospective candidates for neurosurgery or admission to the Neurosurgical Intensive Care Unit in a public sector Hospital. This, however, did not occur. The researcher therefore had to check the theatre list daily for scheduled neurosurgical patients. The candidates who were expected (pre-operatively) to be ventilated post-operatively for more than 48 hours where screened for inclusion into the study. The researcher visited the candidate in the ward, explained the purpose of the study and obtained informed consent. Table 6.2 indicates the number of subjects screened, included, excluded and withdrawn from the study.

In order to assist with the identification of more candidates in the Neurosurgical Intensive Care Unit, the researcher offered a minimal financial gift to the nursing staff, if they contacted the researcher and if the candidate was successfully enrolled into the research. This applied to circumstances where the researcher was not present to identify candidates at night, over weekends or in case of unplanned intubation.

6.5.2.3. Screening of candidates

A total of seventy-one subjects were screened, but not all were enrolled for reasons listed in Table 6.2. (Also see Table 1 in Addendum 2). Reasons for cancellation of surgery was that the intensive care unit did not have any open beds, the patient refused surgery, or patient wanted to come back for surgery and never did. In some cases the subject went to theatre, but the surgery was not performed, due to patient condition or the Neurosurgeon preferred not to perform the surgery, due to patient condition or prognosis.

Inclusion criteria

After consent had been obtained, the subjects and replacement subjects underwent the screening for the inclusion criteria:

The age of the subject (18 years and older)

It was confirmed that the candidate's age was 18 years or older. The age of the candidate was obtained from hospital records or from the candidate himself. Two candidates were excluded regarding this criterion, as they were both seventeen years old.

Expected to be ventilated longer than 48 hours

Often it was expected that the subject would be ventilated for longer than 48 hours, but was extubated post-operatively. In other cases it was expected that the ventilation of the subject would be less than 24 hours, but the end results was ventilation for more than 48 hours. The decision was therefore to include all possible candidates and to enroll those that meet the inclusion criteria.

After the subject met the inclusion criteria, informed consent was obtained from subjects or their families.

Informed consent

According to the Nuremburg Code of 1947, prospective subjects should have the opportunity to decide whether they would like to participate in the study or not (Brink, 1996:38). The Declaration of Helsinki, an official policy document of World Medical Association, directs ethical principles for medical research involving human subjects (ICH Guidelines, 2002:2). These principles together with the additional principles for medical research, combined with medical care, were included in this study. At national level, the National Health Research Ethic Council is responsible to promote, ensure and monitor compliance, by approved ethics committees with relevant legislation, regulation and guidelines (including Guidelines for Good Clinical Practice in the conduct of Clinical Trials on Human participants) in South Africa (Farmovs Parexel, 2000:5).

"Informed" means that the researcher should convey essential information regarding the research to the prospective candidate. *Consent* on the other hand means that the prospective candidate agrees to participate, after the essential information has been conveyed (Burns & Grove, 1997: 209).

According to Burns and Grove (1997:210) the following essential information has to be provided before consent can be obtained:

a) information of research activities,
a) explanation of the purpose of the research,
b) explanation of the procedures,
c) description of risks and discomforts,
d) description of benefits,
e) disclosure of alternatives (this did not apply to this study),
f) assurance of anonymity and confidentiality,

g) compensation for participation in research (compensation did not apply),
h) offer to answer questions,
i) non-coercive disclaimer,
j) option to withdraw and
k) consent to incomplete disclosure (did not apply to this study).

The abovementioned essential information was included in the consent form (except for (k) as it did not apply).

In this study the researcher visited prospective candidates before surgery or when identified for intubation in the intensive care unit. The researcher informed the candidate, spouse, child or parent (if candidate could not personally give consent.) regarding the purpose, procedure, and possible adverse effects relevant to the study, in his mother tongue. If possible, written informed consent was obtained, from the subject. The subject had to explain to a witness the information provided before the witness signed the consent form.

If the subject was unable to provide consent, the consent by proxy was obtained from the mother or father, son or daughter, wife or husband of the subject. When consent was obtained from the family, the same information as mentioned above was provided; they also had to explain the content of the information to a registered nurse, who then signed as a witness. If the family was not available at the bedside, consent was obtained telephonically from the relatives. The same procedure was followed as already mentioned. (See Addendum 3 for *Consent form*s). The consent form was available in Afrikaans, English and South-Sotho. An interpreter explained the purpose, procedure, and possible adverse effects relevant to the study when the subjects were unable to understand Afrikaans or English.

Obtaining informed consent was a time consuming matter. On average, obtaining consent took about one hour. Many candidates were excluded from the research, as obtaining consent from the subject was impossible, due to confusion or a suppression

of consciousness. Most of the time it was impossible to make any contact with relatives. If the subject or the family refused consent, the subject was excluded from the study. Seventy-one subjects or their families gave informed consent. One subject and one family refused consent.

Exclusion criteria

After the subject or the family gave informed consent, the subjects were screened for exclusion criteria. Exclusion criteria were identified by collecting data for the completion of the *Baseline information and final result f*orm (Addendum 4). Subjects were excluded if one of the below mentioned exclusion criteria were identified. Subjects excluded from the study are indicated in Table 6.2.

a) Neutrophyl count of less than 1.6 X 10^9 /L and a lymphocyte count of less than 0.6 9X 10/L

The neutrophyl and lymphocytes count of the subjects were obtained from the full blood count result, sampled before surgery or intubation. Subjects whose full blood count depicted a leukocytosis or lymphocytosis were excluded from the study.

b) Experienced aspiration before or during intubation

Information regarding aspiration of the subject was obtained from the *Anaesthesia Report and intubation* form, which was completed by the physician who intubated the subject.

c) Were diagnosed with ventilator-associated pneumonia before or during intubation

Chest X-rays were taken pre-operatively. The blind investigator evaluated the chest X-rays and the leukocyte count for the presence of pre-existing pneumonia. An endotracheal aspirate was sampled within the first 6 hours after admission to the Neurosurgical Intensive Care Unit.

Criteria for pre-existing pneumonia were the same as the ventilator–associated pneumonia and were diagnosed by the blind investigator (see 1.10.1.2).

d) Expected to be ventilated for less than 48 hours

The researcher obtained telephonically, information regarding the expected period of ventilation from the physician. Later on the researcher also became more proficient in predicting the period.

e) Used antibiotics at the onset of the study

The use of antibiotics at the onset of the study was identified from the subjects prescription charts. The researcher checked the subject's prescription chart for any prescription of antibiotics.

Antimicrobial therapy was routinely prescribed post-operatively, but was not considered as an exclusion criterion as this therapy was not related to pneumonia, but prevention of wound infection.

f) Intubated in another hospital, ward or intensive care unit

Information regarding intubation in other areas than the research site was obtained from patient hospital admission records.

g) Diagnosed with primary lung cancer or lung metastases

The diagnosis of primary lung cancer or lung metastases was obtained from the interview of the subject or family or the physician.

h) Subject in another clinical trial of a drug or device within 30 days prior to entering this trial

Information related to enrollment into another clinical trial 30 days before that date, was obtained during the interview of the subject or family.

i) Diagnosed with cystic fibrosis and tuberculosis

The diagnoses of cystic fibrosis and tuberculosis were obtained from the interview with the subject and family or the physician.

In the absence of exclusion criteria, the subject was enrolled into the study, identified and allocated to a study group. These processes will be discussed under Study Performance (6.6). One subject was excluded from the study due to a low lymphocyte count. During the study process, the subject was screened for withdrawal criteria, listed below.

Withdrawal criteria will be discussed under heading 6.6.8 as the subject had to be observed continually for withdrawal criteria.

6.5.2.4. Sample size

A number of 71 subjects were screened for inclusion and exclusion criteria as potential subjects for this study. Thirty-four subjects were successfully enrolled. The number of seventy-one excluded the patients that were unable to provide informed consent and whose family was not available for this purpose (see Table 6.2 for Sample of research).

Table 6.2: Sample of research

DESCRIPTION OF SAMPLE	SAMPLED	FINAL SAMPLE	NUMBER NOT ENROLLED
Possible candidates who met inclusion criteria	73		
Refused consent	2		
Consent obtained/given	71		
Screened	71		
Individuals in study		34	
Group 1		15	
Group 2		6	
Group 3		13	
Withdrawals			36
Extubated within 24 hours	2		
Extubated post-operatively	20		
Self extubation before 24 hours	1		
Died before 24 hours	0		
Requested withdrawal	0		
Not operated	10		
Pilot study	3		
Exclusion criteria:			
Low lymphocyte count			1

Some of the subjects were not treated surgically for the following reasons: the neurosurgeon selected an alternative non-surgical procedure, subjects refused

operation, the intensive care unit was full, some subjects' CD_4 count was too low for surgery and surgery could cause more harmful effects.

6.6. STUDY PERFORMANCE

Under this heading the following will be discussed: the training of all relevant parties, subject identification, allocation of study groups, devices, intubation of subjects, initial management of subjects, daily management of Figure 6.2 is a flow diagram of the study performance after which a discussion will follow.

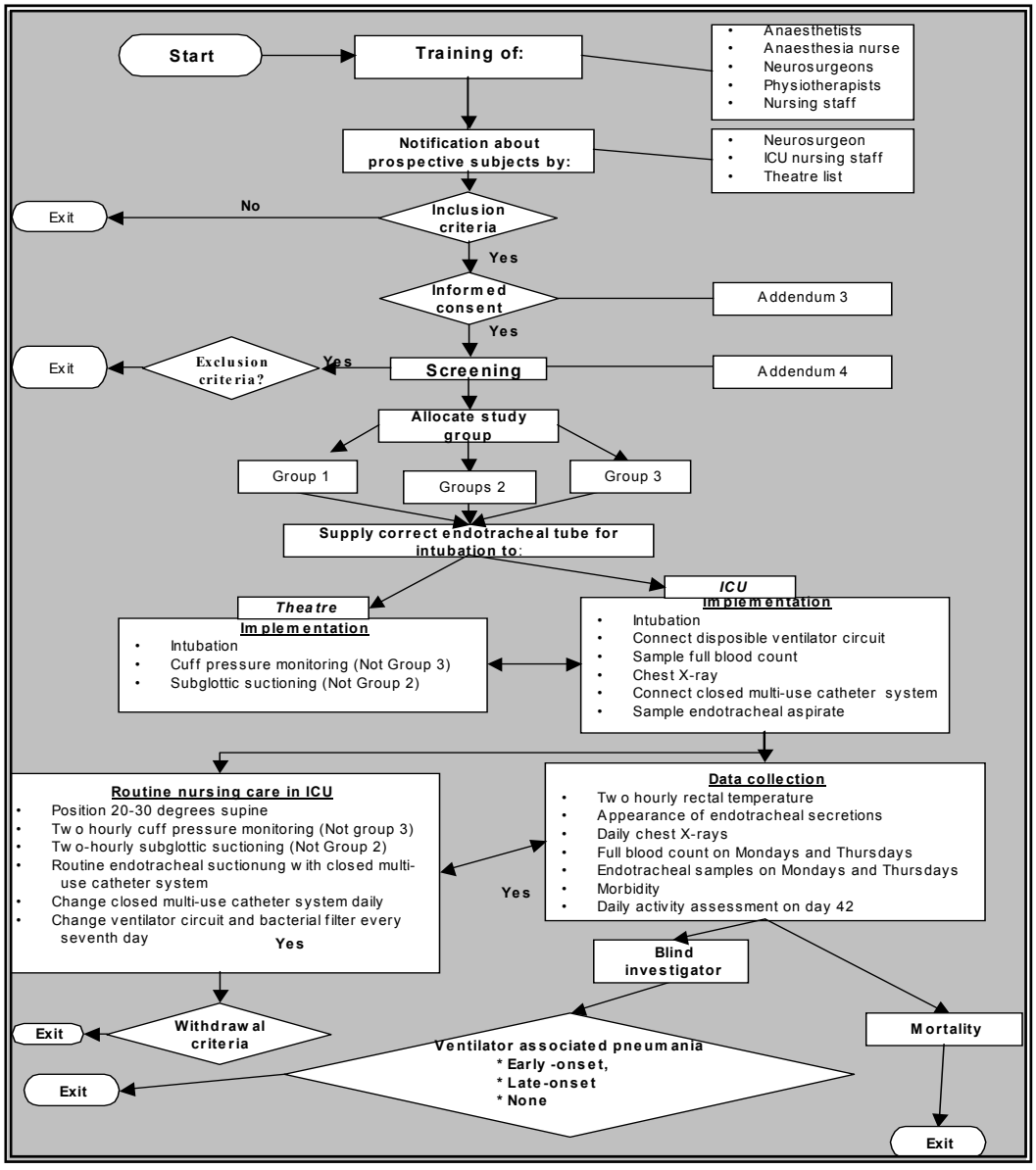

Figure 6.2: Flow Diagram of research implementation

6.6.1. Training of parties involved

Training to the relevant parties will include the following: training of the anaesthetist, anaesthesia nurse, nursing staff, physiotherapists and the neurosurgeons. Addendum 1 contains the content of the training provided to the different parties involved.

6.6.1.1. Training of the anaesthetist and anaesthesia nurse

All the anaesthetists and anaesthesia nurses were initially invited for tea in the theatre tearoom. The purpose, method of and their role in the research were explained. The differences in the endotracheal tubes were demonstrated and the benefits explained. Measuring of cuff pressures was also demonstrated.

The inflation of the Lanz™ valve was demonstrated. The performance of subglottic suctioning was emphasised and demonstrated. The recording of data on the *Anaesthesia Report* form (Addendum 12) was explained.

The research design and Standard Operating Procedure (Addendum 1) were made available to the neurosurgical theatre, in case of further questions. The researcher's telephone number was also available if problems were experienced.

6.6.1.2. Training of nursing staff and physiotherapists

A workshop was held in the tearoom of the Neurosurgical Intensive Care unit. The researcher and the sponsor presented an information session on the purpose of the research. A demonstration of the function, differences and management of the endotracheal tubes was given. A video provided by the sponsor was shown. Samples of the ventilator circuit and closed multi-use suction system were introduced and demonstrated. Procedures like correct positioning of the subjects with the aid of the template (see Addendum1, Figure 2), oral care of the subject, and cuff pressure monitoring were demonstrated and emphasized. Four copies of the *Standard Operating Manual Procedure* (Addendum 1) were provided to the Unit manager to be available at each bedside. After the training session, tea and cake were provided.

These training sessions were repeated for each shift and monthly for the new staff. The researcher also spent frequently time throughout the implementation of the study, individually with those assigned to the subjects. Questions were answered, retraining provided and problems solved.

The same training was provided to the physiotherapists, who also used it as a training opportunity for all their staff and students. As new physiotherapists were assigned to the unit, retraining was provided.

6.6.1.3. Training of the Neurosurgeons

The researcher and sponsor also presented a workshop to the neurosurgeons. The purpose, objectives, inclusion and exclusion criteria of the research were explained. A demonstration of the different types of endotracheal tubes and the management thereof, were presented. The importance of the identification of candidates, was emphasized. The procedure of notifying of the researcher regarding candidates was explained.

The guidelines of the blind investigator, for the prescription of the antimicrobial therapy, were also explained.

6.6.2. Subject identification

After consent had been obtained, the subject was screened for exclusion criteria. The identity of subjects participating in the study was protected by allocation of a study number to the subjects and not by using their true identity. The researcher also made use of the subject's hospital registration number to prevent confusion in the data collection forms which the physiotherapist and nursing staff had to complete (*Daily Procedure* form, Addendum 5).

A record of all subjects screened and enrolled was kept. The subject's initials, first letter of surname and hospital number were recorded against the research number on

a *Record of subject details and study number* (see Addendum 2). Only the researcher had access to this data and the identity of the subjects was therefore protected.

Each patient was identified with a number from 1-57. (Numbers of subjects were not consecutive, because of reduction in subject number after planning of study. Subjects who were withdrawn from the study, were replaced. Not all the subject numbers were utilized due to the reduction of subjects. The numbers that were not used was provided to the biostatistician.

6.6.3. Allocation to study groups

The sampling commenced in April 2003. The implementation phase of the research was delayed, due to delay in the supply of the closed multi-use catheter system. This catheter system was a new product and its importation and its availability was delayed. The implementation continued until 22 July 2004.

The subjects were consecutively allocated to the study groups as indicated in the Table 6.3 below. The order of allocation of subjects to study groups and the number of subjects per group was changed from the initial planning. Firstly, the number of subjects for each study group was reduced from 22 to 15. The original statistics in the planning phase of the study did not reflect candidates that are unable to provide informed consent, due to confusion or suppressed level of consciousness. In most cases, family members were absent to provide consent, although the researcher went to extreme lengths to reach them. Initially a sample size of 66 subjects was planned and eventually only thirty-four enrolled. Table 6.3 indicates the number of subjects included in each study group after re-assessment

Secondly, due to the fact that subjects were not enrolled as planned initially, group 2 and 3, as described in chapter 1, were swapped. This ensured that a “control group” is included in the study in case limited time caused the researcher to terminate the study prematurely before all subjects could be enrolled.

Above-mentioned changes were discussed with the study leader, sponsor and a biostatistician.

Table 6.3: Allocation of subjects to study groups

GROUP ALLOCATION	NUMBER OF SUBJECTS	TYPE OF ENDOTRACHEAL TUBE
Group 1	15	HiLo™ Evac *(Mallinckrodt Medical, Athlone, Ireland).*
Group 2	6	HILO EVAC LANZ ™ *(Mallinckrodt Medical, Athlone, Irelan).d*
Group 3	13	Hi- Contour ™ *(Mallinckrodt Medical, Athlone, Ireland).*

Subjects of group 1 and 3 received subglottic suctioning. Group 2 did not receive subglottic suctioning (this tube is not designed for subglottic suctioning). This type of tube is the standard for intubation at present. The cuff pressures of both groups 1 and 2 were monitored. Group 2 was not completed due to the presence of a confounding variable. This will be discussed later under 6.11.3.4.

6.6.4. The devices

The endotracheal tubes fall into class I group of devices, as they are less hazardous and are subjected to general controls like “good manufacturing practices, labeling, purity, banned devices, recalls recorded, and reports” (Spilker, 1987:141).

The endotracheal tubes are also classified Type II devices. Type II devices are topical devices in nature, as they come into contact with the mucus membrane of the trachea (Spilker, 1987:142).

For the supply, storing, dispensing and specifications of endotracheal tubes and additional devices see *Standard Operating Procedure* (Addendum 1) for management of endotracheal tubes and additional devices (1.7.2).

6.6.5. Intubation of subjects

Under the heading of intubation of subjects, the following will be discussed: the procedures related to intubation in theatre and in the Neurosurgical Intensive Care Unit.

6.6.5.1. Intubation in theatre

The anaesthetist intubated the subjects in theatre prior to the neurosurgical procedure. The researcher provided the correct type of endotracheal tube according to the group assignment (see Table 6.3).

6.6.5.2. Procedures in theatre

The cuffs of Group 1 and 3 were inflated to a pressure of 25 to 33 cm H_2O and were measured and recorded every 2 hours during surgery by the anaesthesia nurse. The cuff of Group 2 (Lanz^{TM} valve system) was inflated with 40 ml of air.

The anaesthesia nurse also performed subglottic suctioning every 2 hours for 8sec. every 20sec. at a negative pressure of 100mgHg, until all secretions were removed. This procedure was only performed in Group 1 and 2 subjects, as the tube used in Group 3 does not allow this function (see Addendum 1 for *Standard Operating Procedure* for intubation).

6.6.5.3. Intubation in the Neurosurgical Intensive Care Unit

When a subject required intubation in the Neurosurgical Intensive Care Unit, the subject was intubated with the endotracheal tube of the specific study group. (The endotracheal tubes were available in a separate marked box with the applicable endotracheal tubes.) All the necessary equipment (ventilator circuits, bacterial filters, rectal thermometers, cuff monometers, closed multi-use catheter system and data forms) was available in the intensive care unit.

After intubation and when the candidate was haemodynamically stable, the nursing staff contacted the researcher. The researcher then obtained consent from the

family. If consent was not obtained, the candidate was not enrolled into the study, but was not extubated. These candidates received the standard nursing care.

6.6.6. Management of the subjects

Preparation of the ventilator and the initial nursing management will be discussed below.

6.6.6.1. Preparation of the ventilator

The preparation of the ventilator involved the connection of a disposable ventilator circuit. Bacterial filters were connected to the inspiratory and the expiratory leg of the circuit. The close multi-use catheter system was connected and covered with a sterile glove to prevent contamination.

In the initial planning, the nursing staff would have prepared the ventilator, as it is part of the standard preparation for any neurosurgical patient. In one situation the ventilator circuit was connected incorrectly. The extension of the closed multi-use system was connected to the wrong end. The incorrect connection extended the distance for the suction catheter and proper suctioning of pulmonary secretions was not possible, as the catheter could not reach deep enough. To prevent a repetition of this mistake, the researcher decided to connect the ventilator circuit and the suction catheter.

6.6.6.2. Nursing management of the subject on admission or after intubation

The subject received the standard nursing care routinely performed on admission to the Neurosurgical Intensive Care Unit. After the subject was stabilized, the following research related tasks were performed.

a) Disposable rectal thermometer was inserted to ensure core body temperature.
b) A blood sample was taken for a full blood count.
c) At the time of the first suctioning procedure (within 6 hours after admission), an endotracheal aspirate sample was collected in a Luki tube and immediately sent

for microscopic analyses and sensitivity testing. If impossible to obtain an endotracheal sample, the sample was collected at the next suctioning procedure. Some of the subjects only came out of theatre after 17:00. The microbiological laboratory closes at 17:00 and the testing would only be performed the following day. Endotracheal aspirates were therefore not collected after 17:00, but the following morning, to ensure a fresh sample reaching the laboratory.

d) Post-operatively a mobile chest X- ray was taken in the Neurosurgical Intensive Care Unit in the anterior–posterior position. The nursing staff checked the position of the endotracheal tube. The distal end of endotracheal tube should be positioned 2 to 5cm above the carina. In case of incorrect positioning, subglottic suctioning was applied to subjects of Group 1 and 2, the cuff deflated and endotracheal tube correctly positioned. Subglottic suctioning was not performed in Group 3, but re-positioning of the endotracheal tube was done if necessary. After repositioning, the cuff was re-inflated to a pressure of 25 to 33cmH_2O or inflated with 40cc of air as applicable.

The researcher visited each subject post-operatively to ensure:

a) correct connection of the equipment;
b) that the humidifier is switched on;
c) that all necessary investigations were performed; and
d) that the staff is familiar with the procedures of the specific study group.

The researcher was also available to help if any problems arose.

The *Standard Operating Procedure* and the *Anaesthesia* form were available in theatre. The *Standard Operating Procedure* and *Daily Procedure form* (Addendum 1 and 5 respectively) were also available at the bedside of the subject and procedures performed were recorded.

6.6.7. Daily management of subjects

The subject received the standard nursing care routinely performed in the Neurosurgical Intensive Care Unit. Table 6.4 tabulates the research-related

procedures, which were performed (see *Standard Operating Procedure* in Addendum 1 for description of procedures). The purpose was to ensure that the procedures were applied constantly, to ensure the reliability of the research and to exclude variables.

Table 6.4: Routine management of intubation

PROCEDURE	FREQUENCY	RESPONSIBLE PERSON	DATA COLLECTION FORM
Maintain cuff pressures between 25 and 33cm H_2O	Two hourly	Nursing staff	*Daily Procedure* form (Addendum 1)
Position patient at 20-30^0 or according to prescription	Continuously	Nursing staff and physiotherapist	Checked daily by using template See Standard operating Procedure Fig. 2
Utilize the closed multi-use catheter system for endotracheal suctioning procedure. Record appearance of secretions	Routinely, when peak airway pressures are increased or in case of audible or visible secretions	Nursing staff and physiotherapist	*Daily Procedure* form (Addendum 1)
Suction subglottic space for 8sec. every 20sec (Smulders *et al.,* 2002:859) at a pressure of 100mgHg until all subglottic secretions were removed	Two hourly	Nursing staff and physiotherapist	*Daily Procedure* form (Addendum 1)
Sample blood for a full blood count	Every Monday and Thursday morning	Nursing staff	*Daily Procedure* form (Addendum 1)
Sample endotracheal aspirate in a Luki tube for microscopic analyses and sensitivity testing	Every Monday and Thursday	Physiotherapist	*Daily Procedure* form (Addendum 1)
Request a chest X-ray	Daily	Nursing staff orders radiographic investigation	*Daily Procedure* form (Addendum 1)
Change disposable ventilator	Every 7 days	Physiotherapist	*Daily Procedure*

PROCEDURE	FREQUENCY	RESPONSIBLE PERSON	DATA COLLECTION FORM
circuit and bacterial filters			form (Addendum 1)

6.6.8. Withdrawal criteria

The following incidences led to withdrawal of the subject from the research:

- the subject was extubated before 24 hours of mechanical ventilation;
- the subject or the family requested withdrawal;
- the subject who was accidentally extubated or self-extubated, or required re-intubation before 24 hours of mechanical ventilation;
- the subject was transferred to another intensive care unit or hospital; and
- the subject who died before 24 hours of intubation and;
- was hypersensitive to cephalosporins, penicillins or carbapenems and required the drug as treatment for ventilator-associated pneumonia.

Each withdrawal criteria will be discussed briefly.

a) The subject was extubated before 24 hours of mechanical ventilation

Subjects who were ventilated for less than 24 hours were withdrawn and replaced with another candidate, because insufficient information was obtained. Twenty-five subjects were withdrawn, due to this criterion. Subjects ventilated between 24 and 48 hours were not withdrawn as they provided information regarding risk factors and causative organisms of early-onset ventilator-associated pneumonia.

Determining pre-operatively how long a subject will be ventilated was extremely difficult, as it often depended on the outcome of the surgery and not due to the development of ventilator-associated pneumonia.

b) The subject or the family requested withdrawal

The subject or the family had the right to request withdrawal from the study at any time. However, no subject was withdrawn due to this reason. None of the subjects

would have been extubated, should they have requested withdrawal. After withdrawal the subject would still have received the standard nursing care.

c) The subject accidentally extubated or self-extubated or required re-intubation before 24 hours of ventilation

In case the subject self-extubated, accidentally extubated, or required re-intubation for some reason before 24 hours of mechanical ventilation, the subject was re-intubated. The conventional endotracheal tubes available in the Neurosurgical Intensive Care Unit were used for re-intubation. The patient received the standard nursing care, after withdrawal. The subject was only withdrawn if accidentally extubated before 24 hours. The subject extubated after 24 hours of mechanical ventilation (due to abovementioned reasons), still provided information contributing to the research. Two subjects were withdrawn due to this criterion.

d) The subject was transferred to another intensive care unit or hospital

If transferred to another intensive care unit or hospital, the subject would not extubated, but would be withdrawn from or did not form part of the study. None of the subjects was withdrawn due to this criterion. The reason for this criterion is that after the transfer it would be difficult to obtain complete information. Data forms, chest X-rays etc. might be lost. This subject was replaced with another.

e) Death that occurs before 24 hours of intubation

Death before 24 hours of intubation was considered as a withdrawal. No subject was withdrawn due to this criterion.

f) Are hypersensitive to cephalosporins, penicillins to carbapenems and require the drug for the treatment of ventilator-associated pneumonia

If the patient required cephalosporins, penicillins or carbapenems for the treatment of a diagnosed ventilator-associated pneumonia and alternative therapy they are selected.

Thirty-six subjects were withdrawn for reasons listed in Table 6.2. Subjects withdrawn from the research due to above-mentioned criteria were replaced. Records of reason for withdrawal was recorded and reported to the Sponsors.

6.7. PILOT STUDY

The pilot study is a smaller version of the study. The purpose is to refine the research design methodology applied to similar subjects, same setting, same data collection and analysis techniques (Brink, 1996:60, 174; Burns & Grove, 1997:52). Some more purposes of the pilot study are to determine the feasibility of the study and to identify unforeseen problems, before the study is implemented (Brink, 1996:60, 174).

The main purpose of the pilot study in this research was, firstly, to evaluate if the nursing staff complied with the procedures and if any problems were experienced with recording of data. The nursing staff did comply with the research design. When problems were experienced, more support and training was provided.

Another purpose of the pilot study was to ensure that the researcher was familiar with the baseline assessment and screening of the subjects. The *Baseline Information and Final Result* (Addendum 4) and *Daily Procedure* form (Addendum 5) were evaluated for insufficiencies, as they were new designs and were untested.

The forms were adequate for measuring purposes, but an additional intubation form was designed for intubation in the intensive care unit, as the *Anaesthesia Report* form was not applicable. (All the data collection forms were developed before the pilot study and were coded in consultation with a biostatistician.)

The implementation of the pilot study is also to identify any flaws in the research design (Joubert *et al*., 1999:52). The researcher realized that close observation should be kept of the anaesthetist, anaesthesia nurse, nursing staff and the physiotherapists. This implied that the subjects should be visited daily.

A pilot study, which included three subjects, was performed at the end of April 2003. The subjects were intubated with the endotracheal tube facilitating subglottic suction. The researcher was familiar with the data collection form. The pilot study provided opportunity to become proficient with the anthropometric measurements. The data of the subjects in the pilot study did not form part of the results of the study.

If any changes are made to the research design after the pilot study, it must be re-submitted to the ethics committee (Joubert *et al*., 1999:52). This was not the case with this study as no changes were made to the research design.

6.8. MEASUREMENT AND DATA COLLECTION

"Measurement is the process of assigning 'numbers to objects'" (Burns & Grove, 1997:51). The instrument is the device that facilitates this process of measurement. Data are divided into the following levels of measurement: nominal, ordinal or ratio level of measurement. Instruments should reflect both reliability and validity (Burns & Grove, 1997:51). Data collection involves generating numerical data to address the research objectives, questions or hypotheses (Burns & Grove, 1997:53).

Data collection was initiated after the candidate was identified and provided consent. The manner in which data was collected in this research and in which data collection forms were used, is summarized in Table 6.5. The table also indicates how the data collection answered objectives of this study.

The initial data collection, after the subject was screened, included completing the data required on the *Baseline Information and Final Results* (Addendum 4) and the *Daily Activity Assessment* (Addendum 7) forms. Information was obtained from the candidate, family member, parent or child. The researcher collected the information before the subject's surgery. This ensured accurate information, as information may be lost due to the effect of anaesthesia or cerebral oedema, if obtained post-operatively.

Demographic data of the subject, contact persons, telephone numbers, age, gender and medical diagnosis was obtained at this time. The purpose for obtaining telephone numbers enabled the researcher to contact the subject or caregivers, if the subject was not seen at the 42-day visit with the neurosurgeon. The 42-day health status was assessed at this point.

A full discussion of the following data follows Table 6.5: baseline and final results, data collection during intubation and data collection during the implementation phase.

Table: 6.5: Summery of objectives, data and related instruments

OBJECTIVES OF RESEARCH	TYPE OF DATA	ADDENDUM AND NUMBER IN INSTRUMENT
Incidence of ventilator-associated pneumonia	Chest X-rays	**Addendum 6** 3. The results of the chest X-ray
	Leukocyte count	**Addendum 6** 2.1. Laboratory results related to the diagnosis of ventilator-associated pneumonia
	Appearance of pulmonary secretions	**ADDENDUM 5** 3. Close suctioning
	Temperature	**ADDENDUM 5** 5. Temperature record
	Microscopic culture and sensitivity result of endotracheal aspirates	**ADDENDUM 6** 2.2 Microscopic culture of endotracheal aspirate

OBJECTIVES OF RESEARCH	TYPE OF DATA	ADDENDUM AND NUMBER IN INSTRUMENT
Risk factors	**Pre-intubation risk factors** Trauma History of chronic obstructive pulmonary disease Smoking Diabetes mellitus Medications suppressing immune system Suppression of consciousness Malnutrition	**Addendum 4** 2. Risk factors 7.Anthropometric assessment
	Medical conditions Previous surgery	**Addendum 4** 1.9 Other medical conditions 1.10 Previous surgery
	Antimicrobial therapy	**Addendum 5** Antimicrobial therapy
	Post-intubation risk factors Presence of nasogastric tube Presence of intracranial device Suppressed level of consciousness Immuno-suppressive therapy Enteral feeding Bronchoscopy performed Nebulization Gastric ulcer prevention	**Addendum 5** 9. Risk factors after intubation
Causative organisms	Endotracheal aspirate culture	**Addendum 6** 2.2.1. Organism cultured 2.2.2. Organism cultured 2.2.3. Organism cultured
Length of stay in the intensive care unit	Date of admission to the intensive care unit Date of discharge from intensive care unit	**Addendum 4** 3.1 Date of intubation 5.6.Date transferred to the ward
Cuff pressures	Two hourly cuff pressure monitoring	**Addendum 5** 2.Endotracheal cuff pressure
Morbidity	Days spend in the hospital Barthel index at screening and on 42-days Location at 42 days	**Addendum 4 and 7** 3.1 Date of intubation 5.7 Date of discharge from hospital Daily activity assessment at screening and 42-days
Mortality	Date of death	**Addendum 4** Date of death

Each instrument used for data collection will be discussed briefly. The sequence of

the discussion will be according to the research process depicted in Figure 6.1 Flow diagram, namely baseline information and final result; data collection during intubation phase, data collection during implementation phase, information for the blind investigator regarding the diagnosis of ventilator-associated pneumonia, morbidity and mortality.

6.8.1. Baseline information and final result form (Addendum 4)

The researcher obtained the following information from the subject or his family after informed consent had been obtained under the headings of demographic information and risk factors. The researcher was responsible for completing the questionnaire, according to the answers provided by the subject or family member. The information was obtained before intubation of the subject in the ward or in the intensive care unit, or telephonically from the family. If the information could not be obtained before intubation, the information was obtained within two hours from the family. Some of the information was also obtained from the subject's records e.g. prescribed antibiotics, date of birth etc.

When information was obtained by interviewing the subject, the researcher used both open-end questions like: "Tell me about your previous illness". The researcher also made use of closed-end questions like: "Did you sustain any trauma in the past two weeks?" Mostly, objective data was used like the subjects temperature, medication, prescribed etc. that did not require communication or interview skills.

The following data that was collected in baseline information and final result form (Addendum 4) is listed below. For detailed information see Addendum 4.

- Demographic information
- Risk factors
  Pre-intubation risk factors
- Intubation information
- Screening criteria
- Withdrawal criteria

- Mortality assessment
- Anthropometrical assessment

(5.2.3.3 in the Standard Operating Procedure explains the procedure of anthropometrical measurement).

See *Standard Operating Procedure* Chapter 5, heading 5.2.3 for data collection by the researcher. This portion explains the assessment of daily activities according to the *Barthel Index.* The assessment of daily activities will be explained under heading 6.8.5 of this chapter (Chapter 6, Methodology).

6.8.2. Data collection during intubation phase (Addendum 12)

During the intubation the *Anaesthesia Report* and *Intubation in the intensive care unit* forms were utilized for data collection during the intubation phase. (See Addendum 12 for more information).

6.8.2.1. Anaesthesia report form

The *Anaesthesia* form did not only record procedures during the operation period, but provided information related to post-intubation risk factors. The anaesthesia nurse completed the *Anaesthesia* form, when the subject was intubated.

6.8.2.2. Intubation in the intensive care unit form

The intubation in the intensive care unit also provided some information regarding post-intubation risk factors. The neurosurgeon completed the information on the *Intubation in Intensive Care Unit* form (Addendum 11) after the subject was intubated and stabilized.

Both these forms provide information related to procedures performed and post-intubation risk factors. Post-operative risk factors like aspiration, route of intubation and positioning during surgery were identified.

6.8.3. Data collection during implementation phase

During the implementation phase, data was recorded on the *Daily Procedure* form (Addendum 5).

6.8.3.1. Daily procedure form

The nursing staff and physiotherapist completed the *Daily Procedure* form, regarding procedures performed according to the research design. Information related to antimicrobial therapy, gastric ulcer preventative therapy and immunosuppressive drugs, level of consciousness, presence of nasogastric tube and intracranial devices, level of consciousness, enteral feeding, bronchoscope and nebulization, were recorded while the subject was intubated.

The level of consciousness was not assessed according to the Glasgow Coma Scale, as the verbal response (one of the elements of the score) cannot be evaluated in the intubated subject. The researcher developed another scoring system (see Addendum 5 9.3) to assess the subject's level of consciousness. A score higher than 21 indicated suppression of level of consciousness or neurological impairment to some degree.

6.8.4. Information for blind investigator regarding diagnosis of ventilator-associated pneumonia (Addendum 6)

A physician (appointed by the sponsor), with the following qualifications M.BChB, M.Med (Int), FCP (SA) and Certificate in Critical Care (SA) was the blind investigator. The blind investigator was responsible for making the diagnoses of ventilator-associated pneumonia, according to specific criteria (see Chapter 1 in 1.9.2).

The blind investigator was also responsible for drawing up guidelines for the treatment of a ventilator-associated pneumonia in subjects of this study (see *Standard Operating Procedure*). The blind investigator was not allowed to see the subject.

A second blind investigator was appointed for circumstances when first blind investigator was unavailable. This second blind investigator had to adhere to the criteria for the diagnosis of ventilator-associated pneumonia. Fortunately it was not necessary to make use of the second blind investigator.

The researcher recorded pertinent data for the blind investigator on the mentioned form. The results will be recorded on the *Information for blind investigator regarding diagnosis of ventilator-associated pneumonia form* (Addendum 6).

6.8.4.1. Laboratory results (Addendum 6)

The following laboratory data was provided to the blind investigator and was the required criteria to make a diagnosis of ventilator-associated pneumonia:

a) Full blood count was evaluated for leucocytosis (a count >$10x10^9$ /L),
b) Microscopic results of cultures and sensitivity of endotracheal aspirate. (The organisms cultured, together with their sensitivities and resistance was recorded on Addendum 6 by the researcher) When the laboratory results indicated that the cultured organism was a contaminant, the result was not recorded.

6.8.4.2. Daily procedure form (Addendum 5)

The appearance of endotracheal secretions was recorded with each suctioning procedure by the person performing the suctioning (any description of clouded secretions, was considered as purulent) and recorded on the *Daily Procedure* form (Addendum 5). The *Daily Procedure* form was made available to the blind investigator when making the diagnosis of ventilator-associated pneumonia.

6.8.4.3. Temperature monitoring (Addendum 5)

Rectal temperature was recorded every 2 hours and measured in degrees Celsius. Nursing staff recorded the temperature on the *Daily Procedure* form (Addendum 5) observation chart. Pyrexia was one of the criteria of ventilator-associated pneumonia and was considered as such when the rectal temperature was higher than 38, 3 ^oC (Cook *et al*., 1998:783).

6.8.4.4. Chest X-rays (Addendum 6)

The chest X-ray was collected and provided together with the *Information for the blind investigator regarding the diagnosis of ventilator-associated pneumonia* form (Addendum 6) to the blind investigator. The blind investigator made the diagnosis of a ventilator-associated pneumonia and recorded it on the *Information for blind investigator regarding diagnosis of ventilator-associated pneumonia form* (Addendum 6 under nr 3, The results of the chest X rays). The chest X-ray was evaluated for new or progressive infiltrate or cavitation.

The chest X-rays, laboratory results, records of subjects' temperatures and appearance of secretions were shown to the blind investigator periodically, by the researcher. The blind investigator could then diagnose the presence or absence of ventilator-associated pneumonia. While the blind investigator reviewed the chest X rays and records, the researcher recorded the findings in Addendum 6 under number 2.3-2.6 and 3.

6.8.5. Morbidity

Morbidity is a condition of being diseased, or the ratio of sick to well persons in the community (Miller & Keane, 1978:636). Health Status and Outcomes Assessment tools were selected. Three types of measures define health: biological functioning, general health and disease specific symptoms and problems. General health assessment was selected for this research, as it measures quality of life regardless of individual characteristics like: age, gender disease or condition (Ware & Dewey, 2000: Online]. In the literature a similar terminology to general health is daily living activities (Mahony & Barthel, 2002: Online).

Activities of daily living were evaluated before surgery at screening and on 42 days post intubation, according to the *Barthel Index* (Mahony & Barthel, 2002: Online) (Addendum 8). It is the standard practice in other research studies to obtain this information at 28 days, which made it impossible to make contact with some of the

subjects. As many patients were not from the local area and did not always have a telephone, it was difficult to contact them at 28 days. The patients were followed up by the neurosurgeons at the outpatients department, six weeks after the operation. The researcher has therefore selected this period for the evaluation of activities of daily living and the location of the patient at this time.

Another measure of morbidity in this research was the intubation period, the days spent in the Neurosurgical Intensive Care Unit, days spent in the hospital and location at 42 days. The abovementioned data was obtained from hospital records, like admission books, patient files and Meditech information system.

6.8.6. Mortality

Mortality was assessed according to date of death and the primary cause thereof. This information was obtained from nursing records, laboratory results, death notice and discussions with the neurosurgeon. The data was followed up to 42 days post-intubation.

6.9. VALIDITY

Validity measures if the manipulation of the independent variables, or treatments, actually caused the effects on the dependent variable(s) (Malhotra, 2002:231). Study validity is divided into 1) statistical conclusion validity, 2) internal validity, 3) construct validity, and 4) external validity (Burns & Grove, 1997:228; Spilker, 1991:314).

Spilker (1991:316) reiterated construct and content validity, but also added criterion, face, discriminant and prospective, simultaneous and retrospective validity. For this discussion only the concepts of Burns and Grove (1997:228) will be discussed, as they are more complete. How it was achieved in this research will be indicated below.

6.9.1. Statistical conclusion validity

The researcher has to determine if the independent and the dependent variables were related and therefore accurately reflected the real world (Burns & Grove, 1997:228).

In this particular study the relationship between subjects intubated with three types of endotracheal tubes and the development of ventilator-associated pneumonia will be studied. There are the threats of drawing false conclusions regarding the presence or absence of a relationship or differences. These possible dangers treats are: 1) low statistical power, 2) violated assumptions of statistical tests, 3) fishing and the error rate problem, 4) the reliability of measures, 5) the reliability of treatment implementation, 6) random irrelevancies in the experimental setting and 7) random heterogeneity of respondents (Burns & Grove, 1997:229).

Possible threats to this particular study are the following: low statistical power, reliability of the measures, reliability of treatment implementation, random relevancies in the experimental setting and random heterogeneity of the respondents.

6.9.1.1. Low statistical power

There is the risk that the sample size of this research is too small because a high risk population group with limited numbers was selected (type II error). The result may be that no significant conclusion can be drawn (Burns & Grove, 1997:229).

In overcoming this particular problem a biostatistician was consulted. In the development of this research, statistics were provided regarding the number of patients presently admitted to the research site and the length of stay in the intensive care unit. These statistics, however, did not reflect the candidates that could not provide consent.

To counter-act this variable, the researcher attempted to enroll all possible subjects to the research. The researcher also attempted to obtain permission from the Ethics

Committee, to obtain consent from the Medical Superintendent for those candidates unable to provide consent for themselves and whose family was not available. This attempt was made as research only benefited the subjects. However, this request was denied. Low statistical power may still pose a threat, due to the confounding variable that reduced the number of subjects in the third group.

6.9.1.2. Reliability of the measures

Technique of measuring has to be reliable to ensure that a true difference be found. This means that it has to measure the same every time. In this research, instruments were used to quantitatively measure data (Burns & Grove, 1997:229).

A pilot study was performed to ensure the feasibility of the research. No problems were experienced during the pilot study to indicate that reliability of measures would not be accurate. Measurements in this research were objective data like: temperature, cuff pressures, appearance of secretions, antibiotics administered, laboratory data, chest X-rays interpreted by only one blind investigator, anthropometric measurements and the Barthel Index and were therefore reliable.

The researcher has consulted with experts in this field, e.g. pharmacologists, physicians, physiotherapists, dieticians, representatives from the sponsor and nursing staff. The researcher has also consulted with experts in research, e.g. a biostatistician, physicians, and nursing fraternity of the University of the Free State for advice, information and input. This information was used to draw up instruments to measure the objectives of the research. The instruments of the study have also been derived from recent literature and relevant research.

The researchers recorded most of the data and this attributed to the reliability of the research. A blind investigator made the diagnoses of ventilator-associated pneumonia. The blind investigator was not aware of the study groups of the subjects. According to Joubert *et al*. (1999:49) blindness is a method to reduce variation and bias.

6.9.1.3. Reliability of treatment implementation

Different people provided treatment in this research (Burns & Grove, 1997:230). This may lead to inaccurate measurements.

In this particular research, different nursing staff, anaesthetists, anaesthesia nurses and the physiotherapists performed the subglottic suctioning and cuff pressure monitoring. Training was provided to all the relevant parties. Training commenced before implementation of the pilot study. Training sessions were run separately for the anaesthetist and anaesthesia nurses, the neurosurgeons, physiotherapists and the nursing staff. These training sessions usually took place in areas where there was little distraction. A video, provided by the sponsor, of the benefits of subglottic suctioning was shown. The training sessions included the aim of the study, display of the equipment used and demonstration of procedures. Time for questions and discussion were allowed. Initially, everybody was quite enthusiastic regarding the research. The delay in the initiation required some of the training to be repeated before the initiation of the pilot study. The researcher also provided training for the night staff of the intensive care unit.

The anaesthetists rotated every month. It became a very laborious and sometimes impossible exercise to train the new anaesthetist monthly. The researcher ensured that the anaesthesia nurse was fully aware of the research procedures and explained the procedures to the new anaesthetist every month. In the absence of the anaesthesia nurse (when on leave or sick leave), the researcher took responsibility for this duty.

The research was implemented over a period of 18 months. On occasion it seemed that some of the research procedures were neglected. The researcher spent individually and corporately time re-training and motivation, especially the nursing staff and the neurosurgeons. It was obvious that some of the nursing staff were more motivated than others to comply with the research design. This was due to a lack of exposure to clinical trials performed by Critical Care nurses themselves. There was

also an element that indicated a resistance towards research, in the case of one registered nurse. The root of this problem was never identified. This however was not the case with all the nursing staff.

The researcher trained all new and rotating staff, to ensure that all subjects received the same treatment. Critical Care students and prospective Critical Care students rotated in the intensive care unit on a monthly basis. The researcher presented training on an individual basis.

A *Standard Operating Procedure* was available as reference at each subject's bedside. Unfortunately very little reference was made to the *Standard Operating Procedure,* as it was often found in obscure places. The staff would rather phone the researcher. The researcher therefore requested a speed dial number that was often utilized.

The researcher also visited the subjects at least once a day to ensure adherence to the research design and to change the closed-multi use catheter system.

6.9.1.4. Random irrelevancies in the experimental setting

Random irrelevancies are any dynamic factors that have an influence on scores (Burns & Grove, 1997:230).

In the intensive care unit any dynamic may influence this particular research. This may include staff that is rotating, unfamiliarity with research, unwillingness to participate in research etc. These factors were discussed under reliability of treatment implementation.

The researcher ensured that the staff understood the reason for the research. Many of the informal discussions with staff members revealed unfamiliarity with research. The researcher continuously discussed issues related to the research with the staff members until they "bought" into the idea. From time to time the purpose of the

research was emphasized to ensure that staff remained motivated to comply with the research design as discussed above. When they were eventually convinced about the benefits to them and to the subject, concerns disappeared.

The researcher was aware of any changes in dynamics as the research was implemented. As new staff was allocated and some of the initial staff allocated to other intensive care units, perspectives related to research changed. In one incident a registered nurse refused to perform the subglottic suctioning and the subject had to be withdrawn from the research. Such dynamics was easily identified as the researcher's office was just next to the Neurosurgical Intensive Care, allowing for easy access to subjects and field workers. Address this variable, the researcher maintained good communication with the staff members and was often informed of changes of dynamics at the research site.

The researcher was also familiar with the research site and with the staff members as the In-service training officer. This limited this threat of random irrelevancies in the practical setting.

6.9.1.5. Random heterogeneity of the respondents

Random heterogeneity of the respondents' threat is related to differences in the subjects (Burns & Grove, 1997:230).

The researcher addressed this "threat" with the inclusion and exclusion criteria. The respondents, who could made the diagnosis of ventilator-associated pneumonia difficult, were excluded from the research. The selected population (neurological and neurosurgical patients) ensured the homogeneity of the study group. This is significantly more than in similar studies that did not mention the diagnosis, or indicate the variety of the diagnosis of the subjects, as some of the studies mentioned in Chapter 5.

The selected population unfortunately influenced the research in another way and this threat had an impact on the research. Obtaining consent from some of the prospective subjects was problematic, due to the fact that the neurosurgical patient may be confused, or their level of consciousness may be suppressed. These candidates could not provide informed consent. In such a case the researcher attempted to contact family members to obtain consent, but these efforts were often futile. The fact that consent could not be obtained from all the possible subjects, excluded those intubated for a longer period.

6.9.2. Internal validity

According to Burns and Grove (1997:230) internal validity is the: “extend to which the effects detected in the study are a true reflection of reality, rather than being the result of the effects of extraneous variables.” The writers list 13 threats to internal validity. According to the researcher the following four threats applicable to this study are: maturity, instrumentation, selection and mortality. These variables will be discussed below.

6.9.2.1. Maturation

As the research progresses, the researcher and those involved become more experienced and wiser (Burns & Grove, 1997:230).

To minimize the effect of unfamiliarity, a pilot study was implemented, to ensure that problem areas are identified and solved before implementation of the research design. The researcher was mainly involved with the recording of data. The fact that the researcher developed the instruments, ensured familiarity with it from the beginning. Implementation of the pilot study resolved any minor problems.

The researcher focused on supporting the nursing staff, as they were primarily involved with data collection during the implementation phase. Everybody involved become more familiar with the procedures before the study was implemented as they were given the opportunity to experiment with the devices of the research. The

subjects enrolled into the research in the beginning received the same management as those enrolled at the end. The nursing staff that rotated monthly was not as familiar with all procedures of the research procedures. This variable was managed as discussed under the heading of “Reliability of treatment implementation”.

6.9.2.2. Instrumentation

Data collectors may become more familiar with the instruments between the pre- and post–test (Burns & Grove, 1997:230).

Pre-and post-testing does not apply to this research, but the risk existed that, as the staff became more familiar with the *Daily Procedure* form, that they might just have recorded values out of habit, but not as a true reflection of the reality. The researcher daily checked the subject’s observation chart and *Daily Procedure* form and compared them with the instrument for irregularities in the recording of the subject’s temperature. Irregularities were not discovered, but incomplete records remained a problem throughout the research. Fortunately, the researcher could recover these data from the patient observation chart or memory bank of the monitor. The staff responsible for incomplete recording of data was addressed, but it did not seem to have a lasting effect in solving the problem. Incomplete recording of data was usually associated with an increased workload in the unit.

Concerning is that performance of procedures (like subglottic suctioning and mouth care) could just recorded without performing it. The opinion of the researcher is that this problem may be limited as the staff was truthful in indicating when a procedure was not performed.

6.9.2.3. Selection

Selection is when randomization is not possible and the process of selection of subject groups influences the research results (Burns & Grove, 1997:231).

In this research subjects were enrolled consecutively and were not randomized. (This method was selected to prevent confusion of nursing staff, regarding the different procedures involved with each study group). Subject selection was performed according to specific inclusion and exclusion criteria. The researcher was responsible for selection of subjects and kept to research design. This variable therefore does not apply.

6.9.2.4. Mortality

Mortality influences research in the way that the subject who drops out may be different from those remaining in the research (Burns & Grove, 1997:231).

Measurement of mortality is one of the objectives of this research. This variable will be considered in the interpretation of the data.

Threats that do not apply to this study are: history, testing, statistical regression, interaction with selection, ambiguity about the direction of causal influence, diffusion or imitation of treatments, compensatory equalization of treatments, compensatory rivalry by respondents receiving less desirable treatments and resentful demoralization of respondents receiving less desirable treatments (Burns & Grove, 1997:230-232).

6.9.3. Construct validity

The process to develop construct validity involves instruments that actually measure the theoretical construct that it is supposed to measure (Burns & Grove, 1997:232).

The diagnosis of ventilator-associated pneumonia is done on criteria already used and recommended by the Centers for Disease Control and Prevention. A blind investigator, who did not know to which study group the subject was assigned to, made the diagnosis of ventilator-associated pneumonia.

Threats to construct validity in this research are the following: mono-operation bias, mono-method bias, interaction of different treatments, and confounding construct. These variables will be discussed below.

6.9.3.1. Mono-operation bias

Mono-operation bias is a risk when only one measure of measurement is used (Burns & Grove, 1997:232).

The diagnostic criteria used in the diagnosis of ventilator-associated pneumonia in this research were not only based on one criterion, but on a set of criteria are recommended by the Centers of Disease Control and Prevention (Thompson, 1995:695).

6.9.3.2. Mono-method bias

More than one measure of a variable was used, but only one method of recording is used (Burns & Grove, 1997:232).

This type of bias was addressed by the different types of measures used like, chest X-rays, core temperature and appearance of secretions recorded on *Daily Procedure form* and laboratory results obtained from central computer system. Each of these measures is very specific and done according to standard procedures.

6.9.3.3. Interaction of different treatments

Different treatments are sometimes selected to treat a subject (Burns & Grove, 1997:232).

This threat did not apply, as one group was completed before the next one was started. Subjects therefore received the same treatment and this variable did not apply to this research.

6.9.3.4. Confounding construct

In the design of a methodology the researcher had to make decisions about the intensity of the variable that would be measured. The intensity of the variable will be reflected in the study. This variable may eventually have an effect on the outcome of the research. A confounding variable may lead to mistaken conclusions. The variable measured does not provide an accurate reflection of the construct (Burns & Grove, 1997:233). Someone referred to a confounding variable as a "dark horse" which seemed an appropriate statement for this research.

According to Joubert *et al*. (1999:50) confounders cannot easily be avoided. Identification of possible confounders is done on the basis of knowledge of the subject. To identify confounders, the researcher has to identify differences in demographic data between subgroups, like age, sex, race, or habits. Confounder can be limited by: 1) matching of cases and controls in case-control studies, precisely according to specific criteria, 2) stratification of the sample in homogeneous subgroups which are then analyzed separately, 3) randomization in a clinical trial in an attempt to make the prevalence of possible confounders similar in the different groups, and 4) advanced statistical analysis such as logical regression.

In this study a confounding variable had an affect on the construct of the research. A new type of anaesthesia drug (remifentanil) was implemented during 2004 in the surgery of neurosurgical patients. The advantage of this drug for the neurosurgical patient lies in the fact that the patient wakes up rapidly post-operatively. The level of consciousness of the neurosurgical patient can be assessed more accurately post-operatively.

Remifentanil is a selective μ-opoid agonist with a rapid onset and a short duration. The drug has a biological half-life of 3 to 10 minutes. In a study of remifentanil, some of the subjects did not experience pain, but they did experience anxiety and agitation as observed in this study. In the study of remifentanil, the subjects required more

sedation together with the remifentanil (Solté, Biedler, Silomon, Schöphflin & Molter, 2001: Online)

A side effect of the drug was that the subjects were very agitated post-operatively and this led to early extubation of the subjects. The use of remifentanil was not standard practice when the research was designed. The anaethetists started using the drug during 2004. The use of remifentanil led to extubation of eight consecutive subjects post-operatively within 24 hours (see Addendum 1). These subjects were therefore withdrawn. The Neurosurgeons and anaesthetist involved felt that since the drug is available and it is the current "best care" they refused to "not use" it. The effect on the study was discussed with the study leader, sponsor and biostatistician where after the decision was made to end the study. The main concern was the financial implications to the sponsor, as each time expensive equipment (endotracheal tubes, ventilator circuits, bacterial filters and closed multi-use systems) was wasted. This variable had its influence in Group 3 into which only 6 subjects were enrolled into Group 3 instead of fifteen.

The abovementioned was not the only reason for discontinuing the study. The second reason was that sometimes subjects could not be enrolled for periods, as candidates did not meet the criteria of the research. Thirdly, time restrictions for the completion of study at Masters level became limited. The fourth consideration was the cost to the researcher to continue as another year's registration fees has to be paid for registration in 2005.

6.9.4. External validity

External validity involves the extent to which generalization of the findings of a sample can be done (Burns & Grove, 1997:234). In studies mentioned in Chapter 5, subglottic suctioning has been tested in general subject groups, but in this particular research it is evaluated in a high risk group. The question still remains if the findings may be generalized for high risk groups.

Under the heading of external validity the following will be discussed: interaction of selection and treatment, interaction of the setting and treatment and interaction of history and treatment.

6.9.4.1. Interaction of selection and treatment

According to Burns and Grove (1997:234) it is sometimes difficult to identify subjects who are willing to participate in research and the sample may not be representative.

The number of neurosurgical patients was limited in this research. All possible candidates were therefore screened and all attempts were made to enroll subjects into the research. Attempts included: the researcher checking the theatre list daily for the next day's planned surgery, visiting the Neurosurgical Intensive Care Unit to identify prospective admissions and intubations. The neurosurgeons and nursing staff often forgot to notify the researcher of prospective subjects. The researcher had to be willing to screen and enroll subjects at night and to cancel all vacations for the period of the implementation of the research.

6.9.4.2. Interaction of the setting and treatment

According to Burns and Grove (1997:234), some hospital settings and organizations welcome nursing research, but others may be resistant.

To overcome any resistance against the research, permission was obtained from the hospital management, the manager of the intensive care units and the supervisor of the Neurosurgical Intensive Care Unit. Nursing staff and physiotherapists were trained, regarding the research procedures. The researcher made use of these training sessions to explain the importance of research like this and to motivate staff to participate.

The researcher did not compensate fieldworkers, but they received a small financial reward for identification of prospective subjects. It became a small "competition" between staff members to identify possible subjects and all was done in good faith.

The researcher often received feedback of what the staff did with their financial gift and it seemed to be appreciated, although the gift was very small.

A breakfast was held for the staff in conjunction with the sponsor at the initiation of the researcher and a similar event is planned for the end of the research. The researcher is planning to give feedback at this point, regarding the outcome of the research, as well as lessons learned during the research. Much interest was shown in this event.

6.9.4.3. Interaction of history and treatment

The history of the circumstances should always be considered as it may influence the treatment of the research (Burns & Grove, 1997:234).

Some of the staff came from a background where resistance was cultured against research. Historically, perception was according to some of the nursing staff, that patients are “experimented” on and that the subject did not benefit from the research. The researcher attempted to build a trusting relationship with the nursing and physiotherapy staff. The researcher allowed the staff to decide for themselves if the subject benefited from the research. This however took a while. Initially the staff only identified the benefit of the closed multi-used catheter system applicable to themselves, as it saved them time during the suction procedure. At some point (different for each staff member), they realized the difference in outcome for the subject and perceptions changed regarding research in general. Staff members were eventually more positive and more willing to participate in the research. Sometimes, there was some arguing about who should be allocated to a subjects of the study, as many volunteered.

The physiotherapists were very positive from the beginning. During their own training, they were exposed to research and some had to plan and implement their own research.

6.10. RELIABILITY

Reliability is the consistency of measure obtained. When determining the reliability, the following aspects are considered: stability, equivalence and homogeneity (Burns & Grove, 1997:327).

6.10.1. Stability

Stability or test reliability ensures that consistency is repeatedly measured. This is usually used in physical measures. Stability is when the same result is obtained when the measurement is performed at different times. One of the ways to ensure stability is to ensure that physical measures are calibrated (Burns & Grove, 1997:327).

In this research instruments used for measurement, like the caliper, cuff manometer and monitors for the measurement of temperature, were calibrated by a biotechnician every 6 months (see Addendum 12). This ensured consistency of measurement.

During the research, needle of the cuff monometer became stuck to the lens of the apparatus. The researcher replaced the cuff monometer with another and sent it back to the sponsor. The sponsor's biotechnician corrected the problem and recalibrated the instrument. This ensured that all cuff manometers were reliable and measured the same value.

The researcher practiced anthropometric measurement with the aid of the dieticians, to ensure correct measurements of skinfolds.

The researcher had to ensure stability of the interpretation of the chest X-rays. The researcher would repeat one of the previously interpreted chest X-rays, to ascertain if the chest X-rays, to evaluate if the same outcome was measured each time, by the blind investigator. The measurement was found to be consistent. The blind investigator was not aware of this method of ensuring reliability.

Most of the data utilized in the research was objective, like male/female, age, anthropometric measurement, etc. (see Addendum 4 to 8 for content of instrument and measures).

6.10.2. Equivalence

Equivalence is related to two observers measuring at the same time. Different observers should obtain the same results (Burns & Grove, 1997:328). Mentioned above, is that data collection was objective and interpretation of data was not interpreted by field workers and therefore observation was hardly influenced by equivalence. Data collection in this research was of concrete values like, risk factors, pre-existing disease, temperature measurement etc.

6.10.3. Homogeneity

Homogeneity of the population is when the research limits extraneous variables to reduce the impact on the study. This strategy may therefore exclude subjects from the research and limit the generalization of the study (Burns & Grove, 1997:239).

This particular research attempted to maintain homogeneity of the subjects as the aim was to evaluate the effect of subglottic suctioning in a high risk group. This means that the generalization can only be in high risk groups. This, however, was the purpose of this particular study.

6.11. ADVERSE EVENTS

The researcher, nursing staff and neurosurgeons monitored the subjects for adverse events. No proven adverse event was noted or reported to the researcher.

In the case of an adverse event, the researcher would decide, with her study leader, if the subject would be withdrawn from the study. The Ethics Committee, and the sponsor would be notified in case of such an event per E-mail. The researcher would discuss the adverse event with the treating neurosurgeon as well as the solution to the problem. In a similar study by Kollef *et al*. (1999:1343) performed on

subjects who had undergone cardiac surgery, no adverse effects were experienced.

The researcher would draw up a report of the date, time, nature, steps taken, study device involved and outcome of each adverse event.

6.12. ANALYSIS OF DATA

Demographic and baseline information were summarized per group. Medians and percentiles summarized numeric variables as the distributions are skewed. Categorical variables were summarized by frequencies and percentages. Changes between baseline and consecutive treatment week information, were summarized per group by medians and percentiles or percentages, as appropriate, and described by means of 95% confidence intervals for the difference between groups.

Changes in daily activities from baseline to 42 days were calculated within and between groups and compared by means of 95% confidence intervals, for the percentage differences.

6.13. ETHICAL ASPECTS AND GOOD CLINICAL PRACTICE COMPLIANCE

Ethical aspects of the study consist of obtaining approval and permission for performance of the study and obtaining informed consent from subjects.

6.13.1. Approval for research

Approval for the research was obtained from the Ethics Committee of the Faculty of Health Science in December 2002. See Addendum 3 for letter of approval from Ethics Committee.

6.13.2. Permission for the research

Written permission for the research was obtained from the Hospital Management. The following managers were notified in writing regarding the research. Permission

from these managers was verbal (see Addendum 3 for these letters).

- Manager of the Intensive Care Unit
- The Neurosurgical Department of the University of Free State
- The manager of the Neurosurgical intensive care unit.

6.13.3. Consent

Consent for inclusion into the study was obtained from the patient or the family and they were informed of:

- purpose of the research,
- possible complications or side–effects,
- subglottic suctioning as an additional action to normal nursing care,
- the fact that the researcher contacted the subjects in about 42 days to complete a questionnaire and to inquire about their health, and
- confidentiality was maintained at all times.

The participation of the patients was voluntary and therefore they could withdraw whenever desired. There was no cost involved to the patient regarding the study, but remuneration for participation did not take place.

The patient or the family signed an informed consent form. In the case of a disorientated patient and whose family was not present, the primary investigator attempted to obtain telephonic consent, signed by a witness of consent given. The subject or the family received a copy of the consent form, together with the telephone number of the researcher, in case of any questions.

6.14. RESEARCHER'S OBLIGATIONS

The responsibilities of the researcher are explained in full in the Standard Operating Procedure in Addendum 1 Chapter 5. The researcher's responsibilities will be discussed below.

6.14.1. Training of participants

All participants received training as explained in 6.6.1. Retraining was provided when the need was identified. This happened from time to time, as staff was away on leave or maternity leave. The researcher also provided training for the rotating staff and Critical Care students on an individual basis. These new staff members were identified at the beginning of the month and were orientated regarding the research procedures.

6.14.2. Obtaining consent, collecting and recording data

The researcher was responsible to obtain consent as explained under the heading of 6.6.2. After informed consent was obtained, the researcher screened the subject and recorded the data. The recording of data is explained in 6.8 of this chapter.

6.14.3. Storing and provision of products

The sponsor was responsible to provide the stock to the researcher. The researcher stored the stock related to the research, in a locked office, while adhering to the guidelines in Chapter 1 of *Standard Operating Procedure*. A record was kept of stock received and used in the research (see Addendum 1).

The researcher kept a record of the correspondence of the research, including that with the company and management of the hospital.

6.14.4. Applying of the research design and adherence of all involved

The researcher was responsible to ensure adherence to the research design at all times. Adherence to the research design was accomplished by training of all participants as described under heading 6.6.1. A Standard Operating Procedure was available at each bedside. The researcher prepared the ventilator for the subjects and then visited them daily. The researcher also ensured that data collection was recorded. The researcher was telephonically available to the field workers in case of

any questions or problems experienced.

6.14.5. Monitoring and reporting of adverse events

The researcher visited the subjects daily to monitor them for any adverse events. The neurosurgeon and the nursing staff were also informed to notify the researcher in case of any adverse events. Fortunately, no adverse events were reported or identified.

6.15. SPONSORS OBLIGATIONS

The following responsibilities of the sponsor have been identified at the planning phase of the research and will be discussed below.

6.15.1. Experts for expert committee and blind investigator

The sponsor identified a physician involved with research for the expert committee. The local representative, who would serve as the coordinator with the company at local level, represented the company and also served as the monitor of the research. The second person represented the management of the company and was responsible for the financial management of the research.

The company identified a physician as the blind investigator. He unfortunately moved soon after the meeting to New Zealand and another blind investigator had to be identified. A second blind investigator was also identified in case of unforeseen events, but was never utilized in the research.

The company also identified an auditor of the research, who was a company employee. The responsibilities of the monitor and the auditor are explained in Chapters 7 and 8 of the Standard Operating Procedure.

6.15.2. Training of the physicians nursing staff

The sponsor was involved with the training phase of the participants. The sponsor provided the breakfast for the initial training phase. The sponsor provided a video that demonstrates the purpose and performance of subglottic suctioning. The monitor assisted with training by explaining the management of the different products utilized in the study. This ensured that the participant's skills mastered the skills required by the research. The monitor was also involved with problem solving, when nursing staff did not comply with the research design.

6.15.3. Provision of products on time

The sponsor was responsible for the products used in the research. Products supplied by the company are listed in Addendum 2.

6.15.4. Quality control

The sponsor appointed a monitor and an auditor whose responsibility it was to ensure proper research procedures and data collection. Research data was monitored for completeness every three months. The auditor visited the site every six months to ensure adherence to the research protocol.

6.15.5. Financial obligations

The sponsor was responsible to provide products and funds as budgeted for in Table 6.7.

6.16. TIMEFRAME

The study commenced end of April 2003 and continued until the end of August 2004. The implementation stretched over a period of 18-months. The timeframe of the research is listed in Table 6.6.

Table 6.6: Timeframe of the research

ACTIVITY	YEAR																								
	2002			2003												2004									
	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT
Preparation of protocol																									
Permission from committees and institutions																									
Training of staff																									
Pilot study																									
Implementation and continuous training																									
Data collection																									
Data analysis																									
Report writing																									
Presentation of paper																									

The gap between January 2003 and March 2003 was due to the delay in the availability of the closed multi-use catheter systems in the country, as it was a new product range. The company was waiting the launching the product before making it available for research purposes.

6.17. FINANCIAL OBLIGATIONS

The company Tyco Healthcare sponsored the study. Financial responsibility of the researcher was to carry the cost of a small incentive to nursing staff for notification of a prospective candidate. Table 6.7 provides an explanation of the research.

Table 6.7: Financial obligations

ITEMS	CALCULATION	REAL COST
COST OF DATA COLLECTION AND END PRODUCT		
Photocopies of data collection forms		R 500.00
Language editing		R 4 000.00
Printing and binding cost		R 3 000.00
Writing of articles		R 8 000.00
DIRECT COST OF SPONSOR		
Training at workshops		R 300.00
Cuff pressure monitoring devices	R 1 489.00 x 3	R 4 467.00
Disposable ventilator circuits	R 391.30 x 44	R 17 217.20
Closed multi-use catheter system	R 543.00 x 80	R 67 440.00
Hi-Contour™ endotracheal tubes	R 55.80 x 20	R 1 116.00
Hi-Lo™ Evac endotracheal tubes	R 185.30 x 26	R 4 817.80
Hi-Lo™ Evac Lanz endotracheal tubes	R 316.10 x 15	R 4 741.50
Disposable rectal probes	R 248.72 x 43	R 10 694.96
Luki tubes	R 12.00x 43	R 516.00
Yankuer suction tips	R 30.32 x 43	R 1 303.76
Sterivent S bacterial filters	R 100.72 x 43	R 4 330.96
Hygrobac S bacterial filters	R 70.48 x 43	R 3 030.64
DIRECT EXPENSES OF RESEARCHER		
Telephone calls		R 100.00
Petrol		R 200.00
Rewards		R 150.00
Total		**R 135 725.85**
Average per subject		**R 3550.74**

6.18. LIMITATIONS OF THE STUDY

The following limitations of the study were recognized.

6.18.1. Small sample size

Only 34 subjects were enrolled into the study. The sample size of this study was small compared to similar studies of Kollef *et al*. (1999:1339) who enrolled 143 subjects, Smulders *et al*. (2002:858) 150 subjects and Vallés *et al*. (1995:179) a total of 190 subjects. One of the previously mentioned researchers also indicated a relatively small sample size as the limitation in their study (Kollef *et al*., 1999:1344).

Although 71 subjects were screened, only 34 were successfully enrolled. One of the reasons for the small sample size was the small population group selected for the

study, specifically, neurosurgical patients. Only a limited number of subjects met the inclusion criteria and for some periods, subjects could not be enrolled.

One of the main factors that limited the sample size was that a decision was taken by the management of the hospital to operate only patients with a good prognosis, due to financial restrictions. Patients with a good prognosis will not be ventilated for as long as those with poorer prognoses. Therefore, this factor limited the time of intubation. The decision to operate only patients with good prospects, also limited the number of subjects enrolled into the study.

Often subjects were disorientated, due to their neurological conditions and informed consent could not be obtained. Family members were rarely available (even telephonically) to provide consent. Some of the potential subjects were even unidentified (e.g. traumatic injury patients) for days after admission. It was usually these subjects who were ventilated for longer periods.

Thirty-seventy screened candidates met withdrawal and exclusion criteria and were withdrawn from the study. It was difficult to determine pre-intubation how long a subject would be ventilated. Therefore all possible subjects who met the inclusion criteria of the research were enrolled, but more than 50% of screened subjects could not be included.

Some of the candidates screened, were extubated too early and required re-intubation a few hours later (readiness for extubation was identified by the neurosurgeon). This implied withdrawal from the study and that the subject had to be re-intubated with the conventional endotracheal tube. It led to wasting of research equipment, such as the closed multi-use catheter system and ventilator circuit. Unfortunately, the subject lost the benefit of these devices and was then at high risk of developing ventilator-associated pneumonia. The early extubation led to the subject being ventilated only for a short period. In some cases the ventilation was less than 24 hours, leading to withdrawal of the subject.

A small sample size may lead to unreliable results (Joubert *et al*., 1999; 28). Furthermore, a small sample may lead to a low statistical power, especially a Type II error. A Type II error occurs when the null hypothesis is not rejected, but there is a difference between the two groups (Burns & Grove, 1997: 422).

6.18.2. Allocation of study groups

The study groups were allocated consecutively to prevent confusion of the staff regarding research procedures. However, random sample selection still remains the mainstay to be included into the sample (Joubert, *et al*. 1999:30).

6.18.3. Diagnostic criteria of ventilator-associated pneumonia

Some studies indicate that the endotracheal aspirates should be obtained with bronchoalveolar lavage (Young & Ridley, 1999:1186). This procedure was not used in this study for the sampling of endotracheal aspirates due to the invasive nature and associated complications (Grap & Munro, 1997:424).

Some researchers emphasize blood positive cultures as part of the diagnostic criteria of ventilator-associated pneumonia. Blood cultures were not used in this study, due to the cost involved with these tests (see 2.5.3.3).

6.18.4. Hourly vs. two-hourly subglottic suctioning

Subglottic suctioning was performed every hour in the study of Mahul *et al*. (1992:24) and Smulders *et al*. (2002: 858). In this study the subglottic suctioning was preformed two hourly as it coincided with routine nursing procedures, to ensure that the subglottic suctioning is not neglected. In some subjects more frequent than two-hourly subglottic suctioning was required. Nursing staff identified this need spontaneously and performed the procedure accordingly. This highlights the lack in the instrument to indicate more frequent subglottic suctioning. In future, studies should identify conditions that require more frequent suctioning of subglottic

secretions. As studies advance some may differentiate between conditions requiring intermittent and continuous subglottic suctioning.

6.18.5. Continuous vs. two hourly subglottic suctioning

Some studies indicated continuous subglottic suctioning. Continuous subglottic suctioning was not used in this study, as only one negative suction inlet was available at each bedside. The researcher was concerned that staff would switch from a low-pressure suction apparatus to a high-pressure suction apparatus, for the endotracheal suctioning procedure and then forget to switch the low-pressure apparatus on again. This omission of change between the two suctioning systems could lead to a period lapsing, during which the subject would not receive subglottic suctioning. The reliability of the study will then be in doubt. In ideal circumstances, continuous subglottic suctioning is the ultimate method.

6.18.6. Limitations identified in instruments

Limitations of the *Baseline Assessment and Final Result* form (Addendum 5) are that the risk factors could have been grouped together. The form could also have been split in two, with the final results separate. However the combination of the two made the final analysis easier.

Complications related to the development of ventilator-associated pneumonia were not identified. The identification of complications was not an objective of the study, but it would have been applicable for recommendations and recognition topics for future studies. One of the observed complications, was the development of hyperglycemia in some of the subjects, due a stress response and use of dexamethazone. Hyperglycemia is one of the high-risk factors in the development of nosocomial infections, including ventilator-associated pneumonia.

The instruments did not offer the option of lateral position during surgery. Fortunately none of the subjects required this option, but is should be considered in future studies.

The following pre-and post-intubation risk factors have not been identified, as some are difficult to identify or measure: alcoholism, acidosis, physical and psychological stress, shock, sleep deprivation, inadequate pain control and upper abdominal and thoracic surgery. Infection control measures like hand washing, poor suctioning procedure and understaffing were also not measured.

6.18.7. Duration of intubation

According to the researcher, the main limitation of the study was the duration of intubation. The mean of duration of intubation of experimental groups one and two and the control group was 27.5, 25.5 and 32.0 hours respectively. The definition of ventilator-associated pneumonia is a pneumonia that developed after 48 hours of mechanical ventilation. However, some of the subjects were ventilated for less than 48 hours. This emphasizes the necessity of a larger sample size.

6.18.8. Single site implementation

The study was implemented in only one intensive care unit and the results may not be applicable to other institutions.

6.19. CONCLUSIONS

The design and methodology were selected to ensure an effective study of the effects of three types of endotracheal tubes on ventilator-associated pneumonia. The study was implemented according to plan. The next chapter depicts the results of the study.

CHAPTER 7

RESULTS

7.1. INTRODUCTION

Chapter 7 reflects the data and results according the objectives of the study. The data was analysed in conjunction with the Department of Biostatistics of the University of the Free State, by means of the SAS® software. The data will be presented in frequencies, percentages, medians for each study group and by comparing the 95% confidence intervals of the study groups. *N* in this study indicates the number of subjects in the study group and *n* indicates the number of subject in the study group who were identified with a specific variable (e.g. n: number of smokers in that study group).

Discussion of data will be under the following headings: allocation of study groups, baseline information, risk factors, number of days spent in the intensive care unit, mortality, morbidity and incidence of ventilator-associated pneumonia.

7.2. ALLOCATION OF STUDY GROUPS

Seventy-one subjects were screened for inclusion into the study. Subjects were selected on the probability that they would be ventilated for longer than 48 hours. Only thirty-four of these subjects were successfully enrolled. Subjects who met the inclusion and exclusion criteria of the research were consecutively allocated to three study groups. Experimental group 1 consisted of 15 subjects (N_{e1}=15), experimental group 2 of 6 subjects (N_{e2}=6) and the control group three of 13 subjects (N_c=13). Allocation to study groups is discussed in the methodology chapter in section 6.5.2.2 (Sampling Process) and Addendum 2 (Record of Subjects enrolled). These thirty-four subjects were studied over a period of 18 months.

7.3. BASELINE INFORMATION

Baseline information included demographic information, neurosurgical procedure or diagnosis, medical condition, previous surgery and lymphocyte,

neutrophyl and leukocyte counts. The researcher obtained baseline data from the subject, or the family of the subject, by means of asking the data required in *Baseline Information and Final Result form* (Addendum 4). Some of the data was obtained from nursing records, prescriptions and assessment on admission forms. Laboratory data was obtained from the Meditech Information System. The researcher took the anthropometric measurement. Where necessary, more clarification of how data was obtained, will be provided under these headings.

The data regarding baseline information is provided in Tables 7.1 to 7.6 and will be discussed below each table according to frequencies and percentages. The percentiles and comparison of the 95% confidence intervals will be described for each study group below the specific table.

Table 7.1: Demographic information

DEMOGRAPHIC DATA	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	F	%	F	%	F	%
GENDER						
Male	5	33.3	3	50	11	84.62
Female	10	66.67	3	50	2	15.38
ALLERGIES						
Penicillin	2	20	0	0	1	7.69

7.3.1. Demographic information

Gender, age and allergies will be discussed under demographic data.

7.3.1.1. Gender

According to Table 7.1, females were predominant in experimental group 1 and in the control group, male was predominant. The gender of experimental group 2 was well balanced. Gender was indicated in literature as a risk factor, due to more smokers in the male population, for the development of ventilator-associated pneumonia (Craven and Steger, 1995:5S).

7.3.1.2. Age

The median age of the subjects in experimental group 1 and 2 are 50 and 51.5 years respectively, indicating that the groups were similar regarding age, but the median of the control group is 37 years.

The 95% confidence interval (C.I.[1]) of comparing the experimental group 1 and the control group is [-1; 21], indicating a tendency of the experimental group 1 to be older. The C.I. of comparing the experimental group 1 and 2 is [-16; 11] and experimental group 2 and the control group is [-4; 23] indicate that these study groups were older.

According to Tasota *et. al*. (1998: Online) patients older than 65 years are susceptible to infections, due to atrophy of the thymus gland and a reduction in cilliary action and cough reflex. The median for their research was much younger than 65 years. In the study of Kollef *et al.,* (1999: 1342) the age of subjects was respectively the same (64.7±12.3 and 62.5 ± 13.1), indicating an older sample than in this study. This indicates that neurosurgical patients are younger than the general population of general intensive care patients.

7.3.1.3. Allergies

As far as allergies were concerned two subjects in experimental group 1 and one in the control group were allergic to penicillin. These three subjects did not develop ventilator-associated pneumonia and therefore did not require antimicrobial therapy with penicillin. On these grounds they were not withdrawn from the study (see withdrawal criteria 1.6.4.3 in Chapter 1). No other relevant allergies were identified.

[1] C.I. indicates in this study 95% confidence intervals for the median difference between the experimental and control groups. Values in brackets refer to those values of the respective groups: [experimental; control]. When the interval includes zero, it is an indication that there may be no difference, in which case the probability, p-value will be larger than 0.05 and the null hypothesis will therefore not be rejected (Joubert *et. al.,* 1999: 81). The numbers above the brackets indicate the study groups compared.

7.3.2. Neurosurgical diagnosis or surgical procedure

The subject's neurosurgical diagnosis was obtained from nursing records and neurosurgical procedures were obtained from theatre reports. The neurological diagnoses were made by the neurosurgeon.

The neurosurgical diagnosis and surgical procedures are listed in Table 7.2 for each study group in frequencies and in percentages. Not all subjects received neurosurgery after intubation, as some had to be stabilised before surgery, in others surgery were not indicated and some died before surgery.

Table 7.2: Neurosurgical diagnosis or surgical procedure

NEUROSURGICAL DIAGNOSIS OR SURGICAL PROCEDURE	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	F	%	F	%	F	%
Clamping of aneurysm	3	20.00	0	-	1	7.69
Anterior fossa tumor removal	0	-	2	33.33	0	-
Removal of meningioma	5	33.33	1	16.67	2	15.38
Hypophysectomy	2	13.33	0	-	1	7.69
Atrio-venous malformation	1	6.67	0	-	2	15.38
Removal of glioblastoma	1	6.67	1	16.67	0	-
Brainstem hematoma	1	6.67	0	-	0	-
Subdural emphyema	0	-	0	-	1	7.69
Rupture of cerebral aneurysm	0	-	1	16.67	2	15.38
Removal of astrocytoma	1	6.67	0	-	0	-
Re-bleeding of aneurysm	1	6.67	0	-	0	-
Status epilepsy	0	-	0	-	1	7.69
Subdural hematoma	0	-	0	-	1	7.69
Removal of extensive tumor	0	-	1	16.67	0	-
Subarachnoid bleeding	0	-	0	-	1	7.69
Intraventicular tumor	0	-	0	-	1	7.69

The conditions of the subjects can be divided into two groups: those that required surgery and those that did not undergo surgery. It is notable that in experimental group 1 the frequency of clamping of aneurysm (n=3) and craniotomy for posterior fossa (n=5) are higher. Neurological conditions and surgery have been identified as a high risk factor for developing ventilator-associated pneumonia. Patients with such conditions are coupled with the supine position and suppression of level of consciousness, also associated with ventilator-associated pneumonia (Craven *et al.,* 1995:5S; Ellstrom, 1999:419).

7.3.3. Other medical conditions

The researcher obtained a medical history during the interview with the subject or the family. Medical conditions were noted if a physician made the diagnoses somewhere in the past. The frequencies and percentages of other medical conditions identified are provided in Table 7.3 per study group. A discussion of the medical conditions will follow below.

Table 7.3: Other medical conditions

OTHER MEDICAL CONDITIONS	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	F	%	F	%	F	%
Hypertension	5	33.33	2	33.33	3	23.08
Previous TB	1	6.67	1	16.67	1	7.69
Hypotension	0	-	0	-	1	7.69
Epilepsy	1	6.67	0	-	1	7.69
Previous stroke	1	6.67	0	-	0	-
Previous head injury	0	-	0	-	1	7.69
History of unstable angina	0	-	1	16.67	0	-

The frequency of hypertension is higher in all groups compared to any other identified condition. Hypertension is not ascribed as a risk factor for the development of ventilator-associated pneumonia, but may be a cause or a symptom in the development of a neurological condition that requires neurosurgical surgery e.g. cerebral aneurysm or subarachnoid bleeding (Hickey, 1997: 569).

7.3.4. Previous surgery

Table 7.4 list the subjects' previous surgery (obtained by the same method as in 7.3.3) in frequencies and in percentages for each study group. The frequencies does not add up to the N per study group as not all the subjects underwent previous surgery and some underwent more than one procedure during their lifetime.

Table 7.4: Previous surgery

PREVIOUS SURGERY	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
	F	F	F
Femur fracture	1	0	0
Previous cranial surgery	1	0	1
Sterilization	2	0	0
Appendectomy	3	0	0
Bladder surgery	1	0	0
Hysterectomy	0	0	1
Repair of rupture of cerebral aneurysm	0	0	2
Cataract operation	0	1	0

The listed previous surgery of the subjects is not significant as most were not associated with the neurological condition. Two surgical procedures are associated with the neurosurgical condition and can be attributed as a risk factor, namely previous cranial surgery and repair of a ruptured cerebral aneurysm.

7.3.5. Lymphocyte, neutrophyl and leukocyte counts

Low lymphocyte and neutrophyl count formed part of the exclusion criteria (see 1.6.4.2.). The purpose of the lymphocyte count was to detect the suppression of the immune system of subjects and to such exclude subjects. The leukocyte count was included to establish a baseline to detect if the subject developed ventilator-associated pneumonia. Table 7.5 compares pre-operative lymphocyte, leukocyte and neutrophyl count according to percentiles per study group. Table 7.6 compares the C.I. for the different study groups.

Table 7.5: Pre-operative lymphocyte, leukocyte and neutrophyl counts

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
LYMPHOCYTE COUNT (1.00-4.00 $X10^9$ /L)[2]			
75% Q3	3.6	2.6	2.1
50% Median	2.5	2.1	1.6
25% Q1	2.1	1.6	1.0

[2] Normal values according to National Health Laboratory Services

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
LEUKOCYTE COUNT (4.00-10.00 $X10^9$ /L)[2]			
75% Q3	13.9	11.1	17.2
50% Median	9.7	10.1	9.6
25% Q1	6.7	7.3	7.3
NEUTROPHYL COUNT (2.00-7.50 $X10^9$ /L)[2]			
75% Q3	11.7	8.20	14.4
50% Median	6.2	7.65	7.6
25% Q1	3.8	6.40	5.0

The mean of the lymphocyte counts were within the normal range, but tended to be to the lower margin of the normal values. The mean of the leukocyte and neutrophyl counts tended to be to the higher limit of the normal values. The leukocyte count was not part of the exclusion criteria and therefore small deviations from the normal values were noted.

Table 7.6: Comparisons of the C.I. of lymphocyte, leukocyte and neutrophyl counts

LABORATORY RESULT	EXPERIMENTAL GROUP 1; EXPERIMENTAL GROUP 2	EXPERIMENTAL GROUP 1; CONTROL GROUP 3	EXPERIMENTAL GROUP 2; CONTROL GROUP 3
Lymphocyte count	[-0.3; 1.6]	[0.2; 1.8]*	[-0.7; 1.6]
Leukocyte count	[-3.6; 15.2]	[-6.7; 3.2]	[-8.8; 3.3]
Neutrophyl count	[-3.7; 3.7]	[-7.5; 2.1]	[-7.9; 3.4]

* *Statistically significant*

The C.I. of comparing the lymphocyte counts indicates that the groups *tend* to be similar. Comparison of the C.I. of the lymphocyte counts of the experimental group 1 and the control groups are *statistically significant different.* However, the difference is not clinically significant.

The comparison of the C.I. of the leukocyte and neutrophyl counts indicated that they were *similar* for the study groups.

7.4. RISK FACTORS

Risk factors are divided into pre-intubation and post-intubation and will be discussed in these two categories.

7.4.1. Pre-intubation risk factors

Pre-intubation risk factors identified in this study are: trauma sustained in the last two weeks, history of chronic obstructive pulmonary disease, smoking presently, diabetes mellitus, previous frequent antibiotic use, steroid therapy, H_2-receptor antagonists, suppression of the level of consciousness and malnutrition. The researcher obtained this information from the subject or the family by taking a medical and drug history and recorded the information on the *Baseline assessment form* (Addendum 4).

Results of pre-intubation risk factors are listed in Table 7.7 and 7.8 as frequencies, percentages and medians for each study group. Results are discussed below each table.

Table 7. 7: Pre-intubation risk factors

PRE-OPERATIVE RISK FACTORS	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	F	%	F	%	F	%
Trauma sustained in the last two weeks	0	-	0	-	2	15.38
History of chronic obstructive pulmonary disease	0	-	0	-	0	-
Smoking presently	8	53.33	2	33.33	6	45.15
Diabetes mellitus	3	20	0	-	1	7.69
Previous frequent antibiotic use	0	-	0	-	0	-
Steroid therapy	2	13.33	0	-	0	
H_2-receptor antagonists	0	-	0	-	0	-
Suppression of level of consciousness according to:						
• Time	5	33.33	2	66.67	8	61.54
• Place	4	26.67	2	50.0	7	53.85
• Person	2	13.33	2	33.33	7	53.85

7.4.1.1. Trauma sustained the last two weeks

Two subjects sustained trauma in the preceding two weeks in the control group. The type of trauma was traumatic brain injury. None of the subjects in the experimental groups sustained trauma.

Three types of trauma are highlighted by literature to increase the risk for the development of ventilator-associated pneumonia namely: burn, severe head and chest trauma (Harris & Miller, 2000:55).

7.4.1.2. History of chronic obstructive pulmonary disease

None of the subjects had any history of chronic obstructive pulmonary disease. According to Lynch (2001:375S), these patients are associated with a higher mortality and are exposed to more frequent antibiotic use.

7.4.1.3. Smoking

Smoking increases oropharyngeal and gastric colonization, increasing the risk for the development of ventilator-associated pneumonia (Harris & Miller, 2000:55). Table 7.7 indicates the number of subjects who smoked and Table 7.8 the number of cigarettes smoked per day.

The frequency of smokers in experimental group 1 was higher than experimental group 2 and the control group (Table 7.7). The median of cigarettes smoked per day by the smokers in experimental group 1 and 2 and the control group were 8, 10 and 2.5, respectively. The number of cigarettes smoked per day in the experimental group 1 tended to be more than the control group, but was not statistically significant with a C.I. of [-17;0] for the two study groups. However, experimental group 1 and 2, and experimental group 2 and the control group are not different according the p-value of the Kriskal Wallis test of 0.79 and 0.24, respectively. One would expect the experimental group 2 (Ne2) to have a higher risk for the development of ventilator-associated pneumonia compared to the other two groups (Harris & Miller, 2000:55), which was not reflected in this study.

7.4.1.4. Diabetes mellitus

Three subjects in experimental group 1 were diagnosed with diabetes mellitus (one subject used insulin and the other two subjects controlled their diabetes with their diet) and 1 subject in the control group also controlled it by means of diet.

7.4.1.5. Indiscriminate use of antibiotics

Indiscriminate use of antibiotic therapy is associated with a higher incidence of ventilator-associated pneumonia (Grap & Munro, 1997:420). Subjects were asked if they often get ill with flue, colds or conditions that require antimicrobial therapy. Conditions that require more frequent antimicrobial therapy like chronic obstructive pulmonary disease and other lung diseases were also considered as indications for frequent antibiotic therapy. Frequent antibiotic use was defined as more than once a year. None of the subjects in any of the study groups used antibiotics on a regular basis.

7.4.1.6. Steroid therapy

Two subjects (13.33%) were using steroid therapy at screening. Both subjects identified dexamethazone as the drug used. Dexamethazone is used in neurosurgical patients to reduce cerebral oedema (Gibbons & Swanepoel, 1995:212). Unfortunately it suppresses the immune system and makes the subject more susceptible to ventilator-associated pneumonia.

7.4.1.7. H_2-receptor antagonist

None of the subjects used H_2-receptor antagonists for the prevention of gastric ulcers. The use of H_2-antagonists is associated with the development of ventilator-associated pneumonia (Grap & Munro, 1997:421). H_2-receptor antagonists changes the pH of the stomach and increase colonization of the stomach. Subjects in this study, who received gastric ulcer preventative therapy, received sucralphate, a drug without the abovementioned side effect. It is the policy at the research site, to prescribe sucralphate, rather than H_2-antagonists, based on recommendations in literature.

7.4.1.8. Suppression of level of consciousness

Level of consciousness was determined according to orientation regarding time, place and person. The subject's level of consciousness in this study was considered to be suppressed if unable to indicated time, place and person. According to Girou *et al*. (1998:1155) suppression of level of consciousness is a risk factor for the development of ventilator-associated pneumonia. The results

indicated a higher degree of suppression of level of consciousness if the person was not orientated according to person, compared to time and place.

As expected higher percentages of disorientation were noted in this study due to neurosurgical subjects selected as population group (Table 7.7). When comparing disorientation according to "person" it is notable the control group consisted of subjects with a higher percentage of disorientation (53.85%) compared to experimental group 1 (13.33%) and experimental group 2 (33.33%).

7.4.1.9. Nutritional status

Malnutrition was assessed with anthropometric measurements as described in the Standard operating procedure, Chapter 5 (5.2.3.3). According to Tasota *et al*. (1998: Online) malnutrition is a risk factor in the development of ventilator-associated pneumonia. The skinfold thickness is a method to determine percent body fat in the clinical setting where it is difficult to determine in any other way (Lee & Nieman, 1993:137) whereas the upper arm muscle area is an indication of the protein reserves (Lee & Nieman, 1993:136). Measurements are expressed as percentiles. The anthropometric measurements were obtained by the researcher at screening and compared with the percentiles of the specific gender (see Addendum 8).

Table 7.8: Anthropometric measurements

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	F	%	F	%	F	%
SUM OF TRICEPS AND SUBSCAPULAR SKINFOLDS THICKNESS						
0 to 5 (Lean)	0		1	16.67	2	15.38
5 to 15 (Below average)	0		1	16.67	4	30.77
15 to 75 (Average)	11	73.34	2	33.34	5	38.47
75 to 85 (Above average)	2	13.33	1	16.67	0	-
85+ (Excess fat)	2	13.33	1	16.67	2	15.38
UPPER ARM MUSCLE AREA						
0 to 5 (Low muscle mass: wasted)	0		0	-	2	15.38
5 to 15 (Below average)	1	6.67	2	33.33	4	30.77
15 to 85 (Average)	6	40.00	1	16.67	6	46.16
85 to 95 (Above average)	3	20.00	3	50.00	1	7.69
95+ (High muscle mass: good nutrition)	5	33.33	0	-	0	-

Sum of triceps and subscapular skinfolds thickness

The sum of the triceps and subscapular skinfolds thickness values of the experimental group 1 and the control group are *statistically significant different* (C.I.[3] [13.0; 39.7]). Experimental group 1 and 2 are also statistically significant different (C.I. [-14; 29]). No statistical difference was found between experimental group 2 and the control group (C.I. [-2; 40]). The non-intubated overweight subject is at higher risk of developing pneumonia (Tufts University, 2000: Online). In the intubated patient, overweight was found to be most predictive to increase the days of ventilation and length of stay in the intensive care unit (Bochicchio, Joshi, Bochicchio, Tracy, & Scalea: 2004: Online). In this study experimental group 1, 26.66%, experimental group 2, 33.34% and the control group, 46.15%, were above average and were therefore at higher risk for the development of ventilator-associated pneumonia.

Upper arm muscle area

Protein depletion is associated with longer-term ventilation and dependence (Thelan *et al.,* 2002:102). And therefore these are patients at risk for the development of ventilator-associated pneumonia. A protein deficient state is

[3] The 95% confidence interval of sum of triceps and subscapular thickness were calculated for the percentage difference.

not so easily identified in the obese patient. Although the obese patient may have above standard muscle mass, the visceral protein stores may be depleted (Hickey, 1997:170).

There was a *tendency* for the experimental group 1 to have higher upper arm muscle area than the control group (C.I.[4] [0; 20]). The comparison of the C.I. of the experimental group 1 and 2 upper arm muscle areas are [-6; 18] and experimental group 2 and the control group are [-4; 18] indicating that these study groups were not different. It is notable that more than ±50% of the subjects reflected above average values in experimental group 1 and 2 in upper arm muscle area, but this is not reflected in the sum of skinfolds.

Some studies did not indicate the assessment of pre-intubation risk factors like assessment of nutritional status, level of consciousness and use of H_2 receptor antagonist pre-operative (Kollef *et al*., 1999:1342; Smulders *et al*., 1992:859; Vallès, *et al*., 1995:181). In fact more reference was made to post-intubation risk factors and taking into consideration pre-intubation risk factors were neglected.

7.4.2. Post-intubation risk factors

Post–intubation risk factors include intubation, duration of intubation period, cuff pressure maintained lower than normal values, mouth care neglected, medical devices, procedures and treatments and antimicrobial therapy.

7.4.2.1. Intubation

Intubation of subjects occurred according to guidelines in Standard Operating Procedure (Addendum 1, Chapter 2). Training was provided to all parties involved in theatre and in the intensive care unit. Intubation was mostly the responsibility of the anaesthetist in theatre and the neurosurgeon on call in the intensive care unit. The anaesthetists rotated every month and therefore the anaesthesia nurse was responsible for the monitoring of the intubation and research procedures during surgery.

[4] The 95% confidence interval for upper arm muscle area was calculated for the percentages.

Subjects were intubated in the theatre (n=26) or in the Neurosurgical Intensive Care Unit (n=8). Intubation data that will be discussed are route of intubation, intubation in theatre and intubation in the Neurosurgical Intensive Care unit and are reflected in Table 7.9.

Table 7. 9: Intubation data

INFORMATION DURING INTUBATION	EXPERIMENTAL GROUP 1		EXPERIMENTAL GROUP 2		CONTROL GROUP 3	
	F	%	F	%	F	%
LOCATION OF INTUBATION						
Theatre (n=26)	13	50	5	19	8	31
Intensive Care Unit (n=8)	2	25	1	12.5	5	62.5
ROUTE OF INTUBATION						
Nasal	0	-	0	-	0	-
Oral	15	100	6	100	13	100
ASPIRATION SUSPECTED						
Yes	0	-	0	-	0	-
No	2	100	1	100	5	100
POSITION DURING SURGERY						
Supine	11	84.62	4	80.00	7	87.50
Prone	2	15.38	1	20.00	1	12.50

Route of intubation

All thirty-four subjects enrolled into the study, were intubated through the mouth, both those intubated in theatre and those intubated in the Neurosurgical Intensive Care Unit. Oral intubation is recommended as nasal intubation contributes to the development of sinusitis (Eggiman & Pittet, 2001:2078; Kollef, 1999:631).

Intubation in theatre

Data collected regarding intubation in theatre and which will be discussed is: aspiration during intubation, position during surgery and duration of surgery.

a) Aspiration during intubation

No aspiration was suspected during the intubation procedure. Due to the use of sedation and anaesthesia, the level of consciousness of the subject is

suppressed. The subject with a depressed level of consciousness is at high risk for aspiration (Harris & Miller, 2000:53).

b) Position during surgery

The supine position is a high risk factor for the development of ventilator-associated pneumonia (Bowton, 1999:30S). Supine positioning during the neurosurgical procedure was used in the majority of subjects, experimental group 1, 84.62%, experimental group 2, 80% and control groups, 87.50%. The prone position allows secretions to run from the mouth and nose during surgery. The anaesthesia nurse noticed this phenomenon. Although an unpleasant idea, one can only postulate that it has a preventative effect in the development of ventilator-associated pneumonia, at least for the period of surgery, as the subject is not aspirating these secretions. The subjects were turned on to their backs after surgery and then the normal mechanisms applied.

c) Duration of surgery

One of the risk factors in this study is the duration of the surgery. The median for the experimental group 1 is 4 hours and 30 minutes, the experimental group 2 is 5 hours and 30 minutes and the control group is 5 hours 15 minutes. The comparison of the C.I. of the experimental group 1 and 2 are [-170; 130], experimental group 1 and the control group are [-142; 80] and the experimental group 2 and the control group are [-180; 150]. The C.I. indicate that there is *no difference* in the duration of surgery of the three groups. Due to the long duration of surgery the control group is at higher risk of silent aspiration as no subglottic suctioning can be performed.

Intubation in the Neurosurgical Intensive Care Unit

The number of subjects intubated in the Neurosurgical Intensive Care Unit were as follows for the experimental group 1(n=2), experimental group 2 (n=1) and control group (n=5). The number of subjects intubated in the Neurosurgical Intensive Care Unit was higher in the control group than in the other two experimental groups. The subjects intubated in the Neurosurgical Intensive Care unit are at higher risk for aspiration, due to the fact that they may not be kept nil per mouth, as compared with the subject that was intubated in theatre.

The subjects who were intubated in the Neurosurgical Intensive Care Unit may also have had a higher risk of aspiration, as deterioration of the level of consciousness may have necessitated intubation. No aspiration in any of the study groups was suspected or observed during intubation in the Neurosurgical Intensive Care unit.

The subjects intubated in the Neurosurgical Intensive Care Unit, were intubated by only two physicians and can therefore not be identified as a significant variable for the 18-month period.

7.4.2.2. Duration of intubation

Duration of intubation was considered from the time of intubation to the time of extubation. In some of the candidates it would include the period during surgery. Duration of intubation is one of the major risk factors in the development of ventilator-associated pneumonia (Grap & Munro, 1997:420). Data of duration of intubation is indicated in Table 7.10.

Table 7.10: Duration of intubation (in hours)

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
75% Q3	53.0	25.50	82.8
50% Median	27.5	25.25	32.0
25% Q1	26.3	25.00	25.5

The subjects were not ventilated as long as had been expected. The control group (N_c=13) had a tendency to be ventilated for a longer period when compared to the experimental group 2, but the 95% confidence interval indicates that this is not statistically significant. The comparison of the C.I. of the study groups are as follows: experimental group 1 and group 2 are [-0.2; 28.0], experimental group 1 and the control group are [-24.8; 16.0], and experimental group 2 and control group are [-62.5; 0.2]. The fact that the subjects of the control group were ventilated for a longer period could indicate the benefit of subglottic suctioning in both the experimental groups.

In the study of Kollef *et al*. (1999:1339) there was no significant difference in the time of ventilation in the group that received subglottic suctioning. Similarly to the study of Kollef and colleagues, the period of intubation was limited.

In the study of Smulders *et al*. (2002:860), the duration of mechanical ventilation was 7.9 ± 9.7 and 7.1 ± 3.4 days in the study group and in the control group respectively. It is clear that the time of ventilation in the study of Smulders and colleagues is significantly longer than in this study.

7.4.2.3. Cuff pressure maintained lower than normal values

Preventative guidelines for ventilator-associated pneumonia indicate maintaining cuff pressure between 25 to 33 cm H_2O (Kollef, 1999:630). Values lower than this will lead to the leaking of subglottic secretions past the cuff, causing ventilator-associated pneumonia. Only the cuff pressures of experimental group 1 and the control group are mentioned as cuff pressure of these two groups were measured. Experimental group 2 had the Lanz™ valve that automatically maintained the cuff pressure within normal limits.

Cuff pressures were measured 2-hourly. Table 7.11 indicate the percentages of the cuff pressures maintained within normal limits or not, during the surgical procedure and in the Neurosurgical Intensive Care unit.

Table 7.11: Cuff pressures maintained within normal limits

CUFF PRESSURES	EXPERIMENTAL GROUP 1 (N_{E1}=15) %	CONTROL GROUP 3 (N_C=13) %
THEATRE (n=26)		
< 25cm H_2O	8.33%	12.50%
25-33cm H_2O	91.67%	87.50%
INTENSIVE CARE UNIT (n=28)		
< 25cm H_2O	6.67%	15.38%
25-33cm H_2O	93.33%	84.62%

Cuff pressures were generally maintained within normal limits (mostly above 80% of the time). However, it is significant to notice that when cuff pressures are measured and not maintained within the normal values, it tends to be lower,

rather than higher than normal values. Cuff pressures lower than normal may lead to the development of ventilator-associated pneumonia.

7.4.2.4. Negligence of Mouth care

According to the research design mouth care should be performed every six hours. Dental plaque has been implicated as the source of pathogens for the development of ventilator-associated pneumonia (Kollef, 1999:632). Table 7.12 indicates the percentage adherence to the prescription.

Table 7.12: Mouth care

MOUTH CARE	EXPERIMENTAL GROUP 1 (N_{E1}=15) %	EXPERIMENTAL GROUP 2 (N_{E2}=6) %	CONTROL GROUP 3 (N_C=13) %
Mouth care routinely performed	86.67%	83.33%	92.31%
Mouth care not routinely performed	13.33%	16.67%	7.69%

Mouth care was maintained in above 80% in all the study groups. The comparison of the C.I. (of non performance of mouth care) of experimental group 1 and 2 is [-44.2%; 24.8%], experimental group 1 and the control group are [-21.7%; 31.0%] and experimental group 2 and the control group are [-20.1%; 49.2%]. The C.I. comparison indicates no difference in the three groups in the non-adherence of mouth care. Reasons for not adhering to the prescription from time to time were not studied and one may only speculate regarding the reasons. Mouth care is such an easy task to neglect, but the preventative effect of the procedure is invaluable for preventing ventilator-associated pneumonia (Harris & Miller, 2000:57).

7.4.2.5. Medical devices, procedures and treatments

Medical devices, procedures and treatments applicable to subjects (Table 7.13) were compared as reflected throughout the intubation period.

The first column indicates the study number of the subject and the second if the subject developed ventilator-associated pneumonia and which type was developed. (√) indicates that the subjects received the specific treatments and

(-) indicates that the subject did not receive that specific treatment. The columns that follow indicate the medical device, procedure or treatment. Unfortunately a linear conclusion of the cause of ventilator-associated pneumonia cannot be drawn, as several risk factors are at play simultaneously. No combination of risk factors that may be the cause of ventilator-associated pneumonia, could be identified.

Table 7.13: Medical devices, procedures and treatments and their association with ventilator-associated pneumonia developed

STUDY NUMBER	TYPE OF PNEUMONIA	TIME OF VENTILATION	NASOGASTRIC TUBE	INTRACRANIAL DEVICE	LEVEL OF CONSCIOUSNESS	IMMUNOSUPPRESSIVE THERAPY	ENTERAL FEEDING	BRONCHOSCOPY	NEBULIZATION	GASTRIC ULCER PREVENTION
EXPERIMENTAL GROUP 1										
1	E	69.5	√	√	√	√	Con	-	-	Suc
2	E	24.7	-	-	-	√	-	-	-	-
3	-	26.5	-	-	-	√	-	-	-	-
4	E	26.3	-	√	-	√	-	-	-	-
5	-	207.0	√	-	√	-	Con	-	-	-
6	-	24.8	-	-	-	√	-	-	-	Suc
7	-	26.5	-	-	-	√	-	-	-	Suc
8	E	49.3	√	-	√	√	Con	-	-	Suc
9	-	27.5	-	-	-	√	Con	-	-	-
10	E	797.0	√	-	√	√	Con	-	-	-
11	-	24.2	-	√	√	√	-	-	-	Suc
12	-	42.0	√	√	√	√	Con	-	-	Suc
13	-	48.5	√	√	-	√	-	-	-	Suc
14	-	56.0	√	-	√	√	-	-	-	Suc
15	-	26.5	-	-	√	√	-	-	-	Suc
EXPERIMENTAL GROUP 2										
23	-	24.8	-	-	-	√	-	-	-	Suc
24	-	25.0	-	-	-	√	-	-	-	Suc
25	-	26.8	√	-	-	√	-	-	-	Suc
26	-	25.5	-	-	√	√	-	-	-	Suc
27	-	25.5	-	-	√	√	-	-	-	Suc
28	-	25.0	-	√	√	√	-	-	√	Suc
CONTROL GROUP										
45	E+ L	145.3	√	-	√	-	Con	-	-	SUC
46	E+L	129.8	√	√	√	-	Con	-	-	SUC
47	-	26.0	√	√	-	√	-	-	-	-
48	E	28.2	-	-	-	√	-	-	-	SUC
49	U	82.8	√	-	√	√	Con	-	-	SUC
50	E	25.5	√	-	√	-	Con	-	-	SUC
51	E	24.5	-	-	-	√	-	-	-	SUC
52	E	24.5	-	-	√	√	-	-	-	SUC

STUDY NUMBER	TYPE OF PNEUMONIA	TIME OF VENTILATION	NASOGASTRIC TUBE	INTRACRANIAL DEVICE	LEVEL OF CONSCIOUSNESS	IMMUNOSUPPRESSIVE THERAPY	ENTERAL FEEDING	BRONCHOSCOPY	NEBULIZATION	GASTRIC ULCER PREVENTION
53	**E**	**32.0**	**-**	**-**	√	**-**	**-**	**-**	**-**	**-**
54	**E**	**49.0**	**-**	√	√	√	**-**	**-**	**-**	**-**
55	**E**	**42.0**	**-**	**-**	√	√	**-**	**-**	**-**	**-**
56	**-**	**25.3**	**-**	**-**	**-**	√	**-**	**-**	**-**	**SUC**
57	**E**	**88.0**	√	**-**	**-**	**-**	**Con**	**-**	**-**	**SUC**

KEYS TO TABLE

E: early ventilator-associated pneumonia

L: late ventilator-associated pneumonia

Con: continuous enteral feeding

Suc: Sucralfate

Time of intubation

The time of intubation has been discussed under 7.4.2.2.

Nasogastric tube

A nasogastric tube was not inserted for all subjects, especially those ventilated for less than 48 hours. The absence of a nasogastric tube may lead to regurgitation of stomach content which may lead to aspiration, which in turn may lead to the development of ventilator-associated pneumonia (Young & Ridley, 1999:1183, 1187).

On the other hand, the presence of the nasogastric tube can also be a contributing factor in the development of ventilator-associated pneumonia, as organisms can colonize on the device (Kollef, 1999:627). Both the subjects that developed late-onset ventilator-associated pneumonia had nasogastric tubes.

Intracranial devices

The number of subjects who received an intracranial device, namely an intracranial pressure monitor, was associated with high percentages of

ventilator-associated pneumonia (33.3% in the experimental group 1, 16.6% in experimental group 2 and 23.1% in the control group). Two of the subjects who received intracranial pressure monitoring, developed late-onset ventilator-associated pneumonia. This may just reflect the seriousness of the condition of the subject justifying use of the device; and not the device as a cause of ventilator-associated pneumonia.

Immunosuppressive drugs

Dexamethazone is the only drug used that can have an immunosuppressive effect (Gibbons & Swanepoel, 1995:212). The drug is often used in the neurosurgical patient to reduce cerebral oedema. In experimental group 1, the use of this drug was associated with 33.3% of the subject receiving the treatment and in control group 50%. The higher percentage in the control group may indicate the positive effect of preventative measures in this study.

Continuous enteral feeding

None of the subjects received bolus enteral feeding, but all those who received enteral feeding received continuous feeding. Bolus enteral feeding is associated with colonization of gram-negative organisms (Young & Ridley, 1999:1191). Continuous enteral feeding poses a lower risk for aspiration (Young & Ridley, 1999:1191).

Bronchoscopy

Bronchoscopy is often used to sample specimens for the identification of the causative organism in ventilator-associated pneumonia. However, this procedure is not without complications (Grap & Munro, 1997:424). None of the subjects received a bronchoscopy.

Nebulization

The use of medication nebulizers has been associated with the development of ventilator-associated pneumonia (Harris & Miller, 2000:55) (see 3.4.2.1). Nebulization was only used in one subject in the experimental group 2. This subject did not develop ventilator-associated pneumonia.

Gastric ulcer prevention

The use of histamine$_2$–receptor antagonists is associated with a higher incidence of nosocomial pneumonia. However, those who used sucralphate had a lower incidence of nosocomial pneumonia (Tasota *et al*., 1998: Online; Young & Ridley, 1999:1191). None of the subjects received this treatment before or after intubation.

7.4.2.6. Antimicrobial therapy

Table 7.14 identifies the number of subjects who received a specific antimicrobial therapy. The fact that the subject received antimicrobial therapy does not indicate that the subject developed ventilator-associated pneumonia. Antimicrobial therapy was also used for other infections like subdural emphyema.

Table 7.14: Post-intubation antimicrobial therapy

ANTIMICROBIAL THERAPY	EXPERIMENTAL GROUP 1	EXPERIMENTAL GROUP 2	CONTROL GROUP 3
	F	F	F[5]
Cephazolin	12	4	8
Amikacin	1	0	0
Cefepime	1	0	0
Penicillin	1	0	1
Chloramphenicol	0	0	1
Metronidazole	1	0	1
Vancomycin	1	0	0
Gentamycin	2	0	0
Ampicillin	0	0	1

The purpose of cefazolin was prophylactic post-operatively for the surgical area. According to Young and Ridley (1999:1193), prophylactic therapy for neurosurgery is acceptable and is not considered as indiscriminate use of antimicrobial therapy.

Indiscriminate use of antimicrobial therapy may lead to resistant organisms and therefore worsening of ventilator-associated pneumonia (Grap & Munro,

[5] Not all subjects received antimicrobial therapy and some received more that one drug at a time.

1997:420). In this study the neurosurgeons prescribing antimicrobial therapy, adhered to the guidelines set by the blind investigator. Treatment was selected according to the organisms identified with microscopic culture and sensitivity testing.

7.5. NUMBER OF DAYS SPENT IN THE INTENSIVE CARE UNIT

According to literature, subglottic suctioning reduces the number of days spent in the intensive care unit (Vallés *et al*., 1995:179). The number of days spent in the intensive care unit was calculated from intubation until transferred to the ward. The results of this study will be discussed below Table 7.15

Table 7.15: Number of days spent in the intensive care unit

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
75% Q3	14	2	9
50% Median	7	2	3
25% Q1	3	2	2

The experimental group 1 had a *tendency* to spend more days in the Neurosurgical Intensive Care Unit than experimental group 2 (C.I. [0; 6]). This was not statistically significant. Both groups were exposed to subglottic suctioning. Experimental group 2 *tended* to spend fewer days in the Neurosurgical Intensive Care Unit than the control group (C.I. [-9; 0]). This can be attributed to the small sample size of the experimental group 2. When experimental group 1 and the control group were compared the C.I. was [–3; 3], indicating no difference in the two groups.

Smulders *et al*. (2002:861) had not found a statistical significant difference in length of stay in the intensive care unit between the subject who received subglottic suctioning and the control group. He ascribed it to the small sample size and this may be why this study also could not identify any difference in the number of days spent in the intensive care unit. It should be noted that the

indication for longer stay in the intensive care unit might be attributed to the neurological condition of the subject.

7.6. MORBIDITY

According to Table 6.5 in the Methodology chapter, morbidity will be measured according to firstly, number of days spent in the intensive care unit and secondly, a comparison between the Barthel index at screening and at 42-days and thirdly, the location at 42 days.

7.6.1. Number of days spent in the hospital

The number of days spent in the hospital is calculated from the day of intubation until the subject was discharged from the hospital. The date of intubation was recorded in Addendum 4 and the date of discharge was obtained from the Meditech Information system. The number of days spent in the hospital is depicted in Table 7.16 and discussed.

Table 7.16: Number of days spent in the hospital

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)	EXPERIMENTAL GROUP 2 (N_{E2}=6)	CONTROL GROUP 3 (N_C=13)
75% Q3	9	3.0	26
50% Median	6	2.5	11
25% Q1	5	2.0	6

Experimental group 1 and 2 did not differ statistical significantly (Kriskal Wallis test, p-value =0.64). Experimental group 1 *tended* to spend fewer days in hospital than the control group, (C.I. [-18; 1]) but this was not statistically significant. The control group tended to spend more days in hospital compared to experimental group 2 (C.I. [-9; 0], however, this was not statistically significant. The lower values of the experimental group 2 may be due to the small sample size of this study group. Comparison of the medians of the different groups, indicate that the control group's stay in the hospital was longer than the experimental groups.

Smulders *et al*. (2002:860) did not find any significance difference in hospital stay in their study and control group.

7.6.2. Daily activity assessment (according to the Barthel Index)

The daily activity assessment according to the Barthel Index is explained in the Methodology (chapter 6, under heading 6.8.5.). The researcher assessed the subjects according to activities, which they could perform and then allocated to each a score according to the Barthel Index. The score is calculated out of a total of 100. The daily activity was assessed at screening and at 42 days. The 42 day assessment was either performed at the neurosurgical outpatients department at the 6 week follow up, or if not possible, they were phone at home. Sometimes the information at 42 days was obtained from a family member, if the subject was not available or unable to speak. Table 7.17 contains the comparison of the percentiles of the Barthel Index scores collected at screening and at 42 days and Table 7.18 compares the C.I. of the Barthel Index scores of the three study groups.

Table 7.17: Daily activity score

PERCENTILES	EXPERIMENTAL GROUP 1 (N_{E1}=15)		EXPERIMENTAL GROUP 2 (N_{E2}=6)		CONTROL GROUP 3 (N_C=13)	
	Screening n=15	42 days n=9	Screening n=6	42 days n=4	Screening n=13	42 days n=11
75% Q3	100	100 95 70	100	97.5	95	100 95 60
50% Median	55		95	80.0	30	
25% Q1	45		5	57.5	0	

Table 7.18: Comparison of C.I. of Barthel Index scores at screening and 42-days

TIME OF ASSESSMENT	EXPERIMENTAL GROUP 1; EXPERIMENTAL GROUP 2	EXPERIMENTAL GROUP 1; CONTROL GROUP 3	EXPERIMENTAL GROUP 2; CONTROL GROUP 3
Screening.	[-50; 50]	[0; 55]	[-5; 95]
42 days.	p-value 0.58	[-25; 10]	p-value 0.64

The diagram below indicates the difference of the three study group's daily activity score (Barthel Index) at screening and at 42-days.

Experimental group 1 and 2 are not statistically significant different at screening (according to the comparison of C.I. [-50; 50]) and at 42 days (according to the p-value 0.58). The experimental group 2's score is less at 42 days compared to at screening. This can only be attributed to a more severe neurological condition at 42 days than at screening. It cannot be attributed to the development of ventilator-associated pneumonia, as none of the subjects developed late-onset ventilator-associated pneumonia.

Experimental group 1 tended to have a higher score than the control group (3) C.I. [0; 55] at screening, but no differences were seen at 42 days (C.I. [-25; 10]). Experimental group 2 and the control group are not different at screening and at 42 days (C.I. [-5; 95] and p-value 0.64 respectively).

7.6.3. Location at 42 days

The location of the subject at 42 days and help required is a good indication of the morbidity of the subjects. In Table 7.19 is a comparison of the location of subjects at 42 days. A total of 24 (n=24) were assessed. The difference in the total number of subjects is due to subjects that had died before 42 days.

Table 7.19: Location of subjects at 42-days

LOCATION AT 42-DAYS	EXPERIMENTAL GROUP 1 n=9		EXPERIMENTAL GROUP 2 n=4		CONTROL GROUP 3 n=11	
	F	%	F	%	F	%
Intensive care unit	1	11.11	0	-	0	-
Ward in research site	0	-	1	25	1	9.09
Rehabilitation centre	0	-	0	-	1	9.09
Home (independent)	3	33.33	1	25	5	45.45
Home (unskilled/ informal help required)	8	55.65	2	50	4	36.36

One subject from each study group was still in hospital at 42 days (11.11%, 25% and 9.09% respectively). It is interesting that a large percentage in all study groups still required help after 42 days at home (see Figure 7.1).

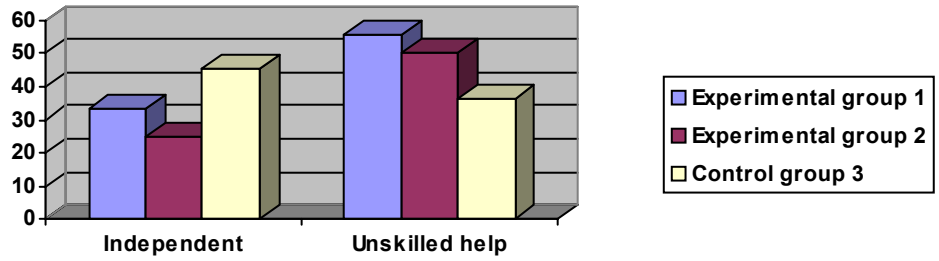

Figure 7:1. Percentage of independent and those requiring unskilled help at home

Although home-based care was not covered in this study, the need for more skilled help for the discharged neurosurgical patient was recognized. Family and friends provided most of the unskilled help and one subject had her own "personal aid".

7.7. MORTALITY

The death of a subject was recorded in Addendum 4. Data regarding the death of a subject was obtained from nursing records, laboratory results, death notice and discussions with the neurosurgeon or family. The subject was only followed up for 42 days. The cause of death was obtained from the death notices. The mortality rate and the causes of death are indicated in Table 7.20 and a discussion will follow below.

Table 7.20: Mortality

CAUSE OF MORTALITY	EXPERIMENTAL GROUP 1 n=6		EXPERIMENTAL GROUP 2 n=2		CONTROL GROUP 3 n=2	
	F	%	F	%	F	%
Respiratory failure	1	16.57	0	-	0	-
Cerebral infarction	2	33.33	0	-	0	-
Cerebral aneurysm	1	16.57	1	50	0	-
Cause of death not determined	1	16.57	0	-	0	-
Brainstem bleeding	0	-	0	-	1	50
Pulmonary embolism	1	16.57	0	-	0	-
Status epilepsy	0	-	0	-	1	50
Raised intracranial	0	-	1	50	0	

pressure						

The mortality rate in experimental group 1 was the highest at 40% followed by experimental group 2 (33.33%) and then the control group (15.38%). The one death that occurred in experimental group 1 was due to respiratory failure. The indication of intubation in this particular subject was respiratory failure. The rest of the deaths in all three study groups were due to neurosurgical conditions. Therefore none of the deaths were caused by ventilator-associated pneumonia. Consequently, mortality could not be evaluated in this study.

7.8. VENTILATOR-ASSOCIATED PNEUMONIA

The blind investigator diagnosed the presence of ventilator-associated pneumonia according to the criteria set in the research design (see Chapter 1, 1.9.2). The incidence and the organisms cultured are listed in Table 7.21. Keep in mind that even if a pathogen is cultured, it may not indicate the presence of a ventilator-associated pneumonia. The subjects who were diagnosed with ventilator-associated pneumonia are indicated by incidence of ventilator-associated pneumonia.

Only group 1 and 3 are compared, as group 2 did not develop ventilator-associated pneumonia. The organisms are indicated in percentage of the total number of organisms cultured on the particular day.

Table 7.21: Ventilator-associated pneumonia data

INCIDENCE OF VENTILATOR-ASSOCIATED PNEUMONIA	EXPERIMENTAL GROUP 1 (n=5)		EXPERIMENTAL GROUP 2 (n=0)		CONTROL GROUP 3 (n=11[6])	
	F	%	F	%	F	%
Early-onset	5	33.33	0	-	9	75.00
Late-onset	0	-	0	-	2	16.67
None	10	66.67	5	83.33	2	16.67[7]
Undetermined	0	-	1	16.67	0	-

[6] The number of subjects do not add to 11 due to some subjects developing both early-onset and late-onset ventilator-associated pneumonia

[7] The sum of individual percentages does not add to total of 100% due to some subjects developing both early-onset and late-onset ventilator-associated pneumonia

7.8.1. Incidence

Ventilator-associated pneumonia was only diagnosed in experimental group 1 and in the control group. The incidence of ventilator-associated pneumonia in the experimental group 1 *tended* to be lower than in the control group, with a C.I. of [-61.5; 0.8].

7.8.1.1. Early-onset ventilator-associated pneumonia

The ventilator-associated pneumonia in experimental group 1 was all associated with early-onset pneumonia and does not reflect the effect of subglottic suctioning. The significance of the number of early-onset ventilator-associated pneumonia, is often neglected in the practical setting as a contributing factor in the development of ventilator-associated pneumonia.

Notable on day 2 is that three types of *Enterobacter* species were cultured. This indicates (at the least) colonization of the airways with organisms that have their origin in the gastro-intestinal tract. If this is true, the subject is at high risk of experiencing aspiration of gastric content before and during the first 24 hours after intubation. This is consistent with the high risk factors of supine positioning (Harris & Miller, 2000:56) during the surgical procedure and suppression of level of consciousness during this period. It might indicate that subjects still experienced aspiration past the endotracheal tube cuff. However, this organism was not identified in samples later on.

7.8.1.2. Late-onset ventilator-associated pneumonia

None of the subjects in experimental group 1 and 2 have been diagnosed with ventilator-associated pneumonia compared to the 2 subjects diagnosed in the control group. The sample size of the study is too small to indicate a significant effect of subglottic suctioning on ventilator-associated pneumonia. The prevention of late-onset ventilator-associated pneumonia in the two experimental groups may even be due to the effect of other preventative measures, like closed suctioning, mouth care and humidification of secretions (see Chapter 4, 4.4.2).

The absence of late-onset ventilator-associated pneumonia in the experimental groups is supported by the study of Kollef *et al*. (1999:1339). His study indicated a 50% reduction in the incidence of ventilator-associated pneumonia.

The question arose if the lack of late-onset ventilator-associated pneumonia in the two experimental groups was related to the application of subglottic suctioning. Consequently, the relative risk was calculated for the three study groups and is depicted in Table 7.22.

Table 7.22: Comparison of relative risks and C.I. [8] for the development of ventilator-associated pneumonia

LATE-ONSET VENTILATOR-ASSOCIATED PNEUMONIA	EXPERIMENTAL GROUP 1; EXPERIMENTAL GROUP 2	EXPERIMENTAL GROUP 1; CONTROL GROUP 3	EXPERIMENTAL GROUP 2; CONTROL GROUP 3
Relative risk	0.4375	0.1750	0.4000
C.I. for the relative risk	[0.0096; 19.9116]	[0.0092; 3.3450]	[0.0221; 7.2525]

As the relative risk values are less than 1 for all study groups (both those receiving subglottic suctioning and those who did not). One can only conclude that in this study subglottic suctioning was not a risk factor. However, the C.I. does not indicate that subglottic suctioning was the preventative factor of the late-onset ventilator-associated pneumonia in the experimental group 1 and 2. One has to consider that the duration of intubation in this study (Table 7.11) was unfortunately too short to draw a conclusion related to the prevention of late-onset ventilator-associated pneumonia, as the confidence intervals are wide. The effect of subglottic suctioning may be more significant when subjects are intubated for longer periods.

[8] A value of 1 indicates that the outcome of the two study groups is the same.
A value larger than 1 indicates the exposure is a risk factor.
A value less than 1 indicates that the exposure is a protective factor.

7.8.1.3. Undetermined subject

The undetermined diagnosis of ventilator-associated pneumonia in the experimental group 2 was a subject with respiratory failure. The cause of the respiratory failure was not determined. No organisms were cultured, but the chest X-ray revealed consolidation of both lungs.

7.8.1.4. Time to the development of ventilator-associated pneumonia

The duration of intubation is longer in those who received continuous subglottic suctioning than in the control group. Subjects did not develop late-onset ventilator-associated pneumonia in the experimental groups. Ventilator-associated pneumonia may have developed later on, but the subjects were ventilated for a short period.

Table 7.23: Time to onset of ventilator-associated pneumonia

DAYS	EXPERIMENTAL GROUP 1 (n=5)	EXPERIMENTAL GROUP 2 (n=0)	CONTROL GROUP 3 (n=11)
75% Q3	0	-	1
50% Median	0	-	1
25% Q1	0	-	0

The median of 0 in the experimental group 1 indicates that the organisms were cultured from the first endotracheal aspirate and this is representative of the 5 subjects that developed early-onset ventilator-associated pneumonia. The comparison of the C.I. of experimental group 1 and the control group is [-2;0], indicating that there is no significant difference between the two study groups.

The same pattern is seen with the control group, but late-onset ventilator-associated pneumonia was identified in the control group compared to none in the experimental groups. As the two subjects developed both an early- and late onset ventilator-associated pneumonia, it is not possible to determine when the late-onset ventilator-associated pneumonia was developed. This however indicates the importance of identification and management of early-onset ventilator-associated pneumonia, as it is a precursor of late-onset ventilator-associated pneumonia.

7.8.1.5. Organisms cultured

The organism cultured is also an indication of the type of ventilator-associated pneumonia (early- or late-onset) that developed (see 2.5.2). Table 7.24 indicate the organisms cultured in this study. The table lists the organisms separately when two organisms were cultured in the same specimen. More organisms were cultured than ventilator-associated pneumonia diagnosed. This is due to colonization of the pathogens, but pneumonia did not develop.

Table 7.24. Organisms cultured

ORGANISMS CULTURED	EXPERIMENTAL GROUP 1		EXPERIMENTAL GROUP 2		CONTROL GROUP 3	
	F	%	F	%	F	%
DAY 1 (FIRST ORGANISM)						
None[9]	4	40.0	2	66.67	0	-
Streptococcus pneumonia	2	20.0	0	-	2	25.0
Klebsiella pneumoniae	1	10.0	0	-	0	-
Haemophilus influenzae	1	10.0	0	-	1	25.0
Enterobacter cloacae	1	10.0	0	-	0	-
Staphylococcus aureus	0	-	0	-	1	25.0
Normal commensal flora	1	10.0	1	33.33	1	25.0
DAY 2 (FIRST ORGANISM)						
None	1	16.67	2	66.67	1	11.11
Streptococcus pneumonia	1	16.67	0	-	0	-
Haemophilus influenzae	1	16.67	0	-	2	22.22
Enterobacter cloacae	1	16.67	0	-	0	-
Staphylococcus aureus	0	-	0	-	1	11.11
Enterobacter	1	16.67	0	-	0	-
agglomemerans	0	-	0	-	1	11.11
Enterobacter aerogenes	1	16.67	1	33.33	4	44.44
Normal commensal flora	0	-	0	-	0	-
DAY 2 (SECOND ORGANISM)						
Escherichia coli	0	-	0	-	1	50.0
Staphylococcus aureus	0	-	0	-	1	50.0
DAY 3 (FIRST ORGANISM)						
None	1	25.0	0	-	0	-
Haemophilus influenzae	1	25.0	0	-	0	-
Normal commensal	2	50.0	0	-	0	-
DAY 4 (FIRST ORGANISM)						
None	1	100.0	0	-	0	-
Streptococcus pneumoniae	0	-	0	-	1	100.0
DAY 4 (SECOND ORGANISM)						
Streptococcus pyogenes	0	-	0	-	1	100.0
DAY 4 (THIRD ORGANISM)						
Haemophilus influenzae	0	-	0	-	1	100.0

[9] None: Microscopic results indicated that no organisms were culture form the specimen

ORGANISMS CULTURED	EXPERIMENTAL GROUP 1		EXPERIMENTAL GROUP 2		CONTROL GROUP 3	
	F	%	F	%	F	%
DAY 5 (FIRST ORGANISM)						
None	1	100.0	0	-	0	-

The number of organisms cultured during day 2 to 5 declined in the experimental groups and not that drastically in the control group. The reduction indicates that the removal of secretions reduced the possibility of colonization.

Most of the organisms that were cultured were gram-positive organisms (community-acquired organisms) associated with organisms related to early-onset ventilator-associated pneumonia. No gram-negative organisms or organisms associated with late-onset ventilator-associated pneumonia were cultured. Organisms such as *Pseudomonas aeruginosa, Acinetobacter baumanii* and *Klebsiella pneumoniae* were predominant organisms cultured at the research site during the same period of the study. These organisms were cultured during the same period in patients not enrolled into this study. The closed multi-use suction system prevented cross contamination from infected patients to research subjects.

According to Kollef *et al*. (1999:1343) subjects receiving continuous subglottic suctioning were less likely to be infected with *H. influenzae* and *S. aureus*, but the difference was not statistically significant. It was not noticed in this study and these organisms were identified in the experimental group 1.

7.9. CONCLUSIONS

This chapter provided results, the discussion of the data analysis and conclusions. The main benefit of this study, although a small sample size, investigated benefits of subglottic suctioning and cuff pressure management in the prevention of ventilator-associated pneumonia and specifically in the high risk neurosurgical patient.

Late–onset ventilator-associated pneumonia has been prevented in the experimental groups. According to the relative risk results, the prevention of

late-onset of ventilator-associated pneumonia cannot solely be totally attributed to subglottic suctioning. Another preventative measure included in the research design, may also have prevented late-onset ventilator-associated pneumonia in the subjects.

A factor that could have contributed to the prevention was a shorter time of intubation in the study groups. Unfortunately, it was not possible to compare the time of intubation of patients who were not enrolled in the study, with those in the study. It “seems” to the researcher that the patients, who were not enrolled into the study during the same period, were ventilated for longer periods and eventually developed late-onset ventilator-associated pneumonia. Multi-resistant gram-negative bacteria were observed in patients not enrolled in the study. Factors that may have played a role are shorter period of intubation, routine mouth care, the use of the closed multi-use catheter system and disposable ventilator circuits. According to the researcher, one of the factors that could have contributed significantly to the prevention of late-onset ventilator-associated pneumonia is the fact that health care providers in theatre and in the intensive care unit were trained regarding preventative measures. They were also “forced” to take specific measures and record the measures. A conclusion that can be drawn from this study is that the key in the prevention of ventilator-associated pneumonia may not be in one strategy, but is to utilize all preventative strategies stringently.

There were no significant differences in the outcome in the morbidity and the mortality of the subjects in the experimental and the control groups.

The next chapter is a discussion of the recommendations of the study.

CHAPTER 8

RECOMMENDATIONS

8.1. INTRODUCTION

Nursing research dates back to the days of Florence Nightingale. Scientific nursing research evolved very slowly (Hodge, Kochie, Larsen & Santiago, 2003: Online). Reality, however, reflects that nurses rather relied on other sources of knowledge such as practical experience, due to lack of scientific research. The result is that implementing research findings in the practical setting remains a challenge, as many barriers still exist. One of the main barriers is the fact that clinical research in the intensive care unit is still limited in the South African context. Measures to breach the gap between research and practice should be seen as a challenge for the nursing profession.

This chapter will discuss challenges identified during implementation of the study, attitude of nursing staff towards research and recommendation regarding possible further research.

8.2. CHALLENGES IDENTIFIED DURING IMPLEMENTATION

The following was identified as challenges during the implementation of this study.

8.2.1. PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA

On implementation of this study, the lack of knowledge of nurses and physicians regarding evidence-base practices in the prevention of ventilator-associated pneumonia was notable. This was confirmed by comments made by health care practitioners that some of the strategies “seems” just too simple to make a difference. It is recommended that both nursing as well as medical staff should be educated regarding the importance of evidence-based practices.

Ventilator-associated pneumonia is associated with an increased mortality, morbidity and medical cost (Harris & Miller, 2000:51, 56). Nursing researchers should play a leading role in development of preventative measures regarding ventilator-associated pneumonia. Strategies to prevent ventilator-associated pneumonia should include the following: availability of the appropriate endotracheal tubes, development/refinement/implementation of a risk assessment tool, importance of appropriate oral care, limiting the period of intubation as well as a change of the name of ventilator-associated pneumonia.

8.2.1.1. AVAILABILITY OF THE APPROPRIATE ENDOTRACHEAL TUBES

It is recommended that high risk patients (patients intubated for longer than 48 hours) should be intubated with an endotracheal tube that facilitates subglottic suctioning as one of the most significant preventative measures in the prevention of ventilator-associated pneumonia is subglottic suctioning and prevention of micro-aspiration (Grap & Munro, 1997:436).

Endotracheal tubes that facilitate subglottic suctioning should be available in all departments where intubation is performed including ambulance services, intensive care units, theatres, emergency departments and wards.

8.2.2.2. PREVENTATIVE STRATEGIES

Education of health care providers, the patient and family is vital in order to address endogenous sources of ventilator-associated pneumonia. All these parties should understand and be able to recognize the risks associated with endotracheal and nasogastric tubes.

It is recommended that strategies to reduce host-related as well as treatment-related factors should be incorporated in general and departmental policies or in other research designs as each of the mentioned preventative strategies is important and should not be neglected.

Standard or universal infection control measures should address the exogenous sources of ventilator-associated pneumonia. It is recommended that hand washing; barrier protection; appropriate disinfection or sterilization of equipment

should be optimised to limit these exogenous sources of ventilator-associated pneumonia.

8.2.2.3. RISK ASSESSMENT TOOL

The need for the development of a more comprehensive scoring instrument that scores the risk of a patient to develop ventilator-associated pneumonia exists. The Omega Scoring System (Girou *et al*., 1998: 1153) has been developed, but is not widely utilised. However some of the risk factors mentioned in this study do not feature in this scoring system.

A more comprehensive scoring tool can be utilised to allocate limited resources to those patients who are at risk for the development of ventilator-associated pneumonia. It is recommended that such a tool should be able to determined different levels of preventative measures for different categories of risk levels.

8.2.2.4. ORAL CARE

Dental plague has been implicated as a source of ventilator-associated pneumonia. Colonization of dental plague could increase the stay of patients in the intensive care unit with up to ten days (Fourrier, *et al.* 1998:305, 307). This was confirmed by data gathered in this study indicating that oral care is often neglected in intensive care units.

A method and frequency of oral care that will prevent colonization of the mouth and ventilator-associated pneumonia should be developed, as increased oral colonization definitely increases the possibility of the development of ventilator-associated pneumonia.

8.2.2.5. LIMITING THE INTUBATION PERIOD

A relation between the time of intubation and ventilator-associated pneumonia exist. Strategies in the prevention of long-term ventilation such as prevention of over sedation, complications of bed-rest, iatrogenic complications, prevention of

malnutrition and electrolyte imbalances should be managed in order to reduce the possibility of ventilator-associated pneumonia.

During the implementation of this study a new anaesthetic, remifentanil was introduced. One of the advantages of this drug is that patients are extubated much earlier due to the short half-life of this drug.

8.2.2.6. IDENTIFICATION OF EARLY-ONSET VENTILATOR-ASSOCIATED PNEUMONIA

A large percentage of subjects are admitted to the intensive care unit with an existing early-onset ventilator-associated pneumonia. This condition is often not diagnosed until the patient is admitted to the intensive care unit.

Early identification of early-onset ventilator-associated pneumonia will require sampling of endotracheal aspirates screening of laboratory results and chest X-rays for evidence of the presence of infection. It is recommended that this become part of the routine management of intubated patients.

8.2.2.7. TERMINOLOGY

One of the challenges that resulted from this study is the correction of the term "*ventilator-associated pneumonia".* This term is misleading due to the fact that the ventilator as such does not contribute to the development of this type of pneumonia. It is recommended that the term should rather be changed to "intubation-related pneumonia" or "endotracheal tube related pneumonia" as these terms reflect the cause of this type of nosocomial pneumonia.

8.2.2. LACK OF EVIDENCE-BASE PRACTICE

The researcher identified the following research topics for future investigation:

8.2.2.1. VENTILATOR CIRCUITS

It is regular practice to change ventilator circuits every seventh day, although it should also be changed when visibly soiled by pulmonary secretions, vomit or blood. In the prevention of introducing organisms to the lower respiratory tract, it

is important that there is strict adherence to infection control principles and isolation techniques (Harris & Miller, 2000:63). It is also recommended that single use ventilator circuits rather than re-usable circuits be used, as cleansing through a pasteurization process is not always an effective way of sterilization. When re-usable ventilator equipment is used, policies should outline the process of pasteurization, disinfecting and maintenance of respiratory equipment.

Nurses should protect their hands and also their eyes, clothes and mouth by wearing gloves, protective glasses, plastic aprons and masks during the changing of ventilator circuits. Strict adherence to infection control principles and isolation techniques is recommended.

The ventilator circuits should be kept free of condensate, as it provides a medium for the growth of bacteria. Draining of the circuits should take place downward away from the patient, to prevent contaminated condensate running down the endotracheal tube (Young & Ridley, 1999:1191). The ventilator circuits should be positioned lower than the patient level to prevent the same consequence. When the patient's position is changed, the same care should be taken to prevent contaminated condensate running down the endotracheal tube. The ventilator tubing should always be correctly positioned and secured by the ventilator arm. The position of the ventilator circuit should be in such a way to prevent back flow of condensate into the patient's airway (Quirke & French, 1996:279).

When water does accumulate in the circuit, it should be drained into a water trap that can be opened and emptied. These water traps are spring-loaded and when opened the circuit's integrity will not be breached. If condensation does take place, draining of the circuit should take place before the patient is turned. Critical care nurses should wear gloves when water traps are emptied and strict adherence to infection control principles and isolation techniques should be practiced. The critical care nurse should be knowledgeable about unnecessary manipulation and disconnection of ventilator tubing as it is detrimental to the patient and should be kept to the minimum.

It is recommended that sterile water, rather than distilled water should be used in the reservoirs as *Legionella* may survive at high temperatures.

8.2.3.2. CUFF PRESSURE MEASUREMENT

Correct cuff pressure maintenance is important for two main reasons. It firstly prevents, pressure necrosis of the inner wall of the trachea and secondly prevents the leakage of subglottic secretions past the endotracheal tube cuff. In usage of the aneroid cuff manometer human influencing factors play a definite role due to lack of management of cuff pressure. The Lanz ^{TM} valve is a pressure-regulating device that is attached to the pilot balloon of the cuff. In circumstances where long-term intubation is expected, endotracheal tubes specifically designed with the Lanz ^{TM} valve should be utilized. The Lanz ^{TM} valve is inflated with 40 cc of air and will maintain the cuff pressure from 25 to 33 cm H_2O. The Lanz ^{TM} pressure-regulating valve automatically regulates pressure by expansion and contraction of the balloon (Mallinckrodt Medical, 2000). It is recommended that future clinical trials regarding this type of device should be considered.

8.2.3.3. SUBGLOTTIC SUCTIONING PROCEDURE

The best procedure for subglottic suctioning should still be established, as two methods presently exist namely, intermitted or continuous. Both these methods should still be studied for complications, user friendliness and consistency of application of the method. The ideal procedure should be compatible for all types of equipment and any hospital settings. Future research is recommended.

8.3. ATTITUDE OF STAFF

The researcher noticed how active nurses are in the United States regarding clinical research. Nurses were listed as researcher on their own and as member of a research team. However, this is not the case in South Africa.

The lack of insight into the importance of nurses performing clinical research was very obvious during this study. Critical care nurses should be encouraged to perform smaller and larger scale research projects to identify for themselves the

benefits of clinical research for their patients. Frequent exposure and seeing the benefit in patients will break down the existing resistance and insecurities.

8.4. FUTURE STUDIES

The researcher implemented a number of preventative strategies, but research has not proved which strategies are critical in prevention of ventilator-associated pneumonia. Further research is necessary regarding catheter systems, preventative strategies, as well as the Lanz™ valve and subglottic suctioning.

The researcher found that the subjects received more frequent endotracheal suctioning compared to patients that were not enrolled in the study (received open suction method). This can be attributed to the ease of the procedure with the closed multi-use catheter system. However, the reasons for this still have to be determined as removal of excessive amounts of pulmonary secretions attributes to the prevention of ventilator-associated pneumonia.

In the study of Deppe, Kelly, Thoi, Chudy, Longfield, Ducey, Truwit and Antopol, (1990:1393) the same phenomenon was found. Although the article is fairly old the significance of the finding must not be underestimated. The mentioned authors found more colonization of the airways with frequent endotracheal suctioning occurred, but it did not lead to a higher incidence of ventilator-associated pneumonia. This emphasizes the importance to determine if more frequent endotracheal suctioning contributes to the development of ventilator-associated pneumonia or does it prevent to it.

According to the researcher, the value of the closed multi-use suctioning system is rather when the patient develops a ventilator-associated pneumonia that it prevents pathogens from the airway to contaminate the environment and prevents cross-contamination of other patients. The effectiveness of this deduction should still be established in research.

Theoretically, closed multi-use suctioning system encloses the subject's airway from exogenous sources of pathogens especially cross-contamination. However, this has not been established in research.

Not all preventative strategies proved to be equally effective. Future studies should determine those strategies that are critical for the prevention of ventilator-associated pneumonia as many strategies are suggested to be effective.

Although the researcher tried to calculate the direct cost for this study, it is recommended that cost analysis of the actual cost effectiveness of preventative measures should be performed in the South African setting. According to the researcher, the direct and indirect cost related to ventilator-associated pneumonia is significant and it is therefore important that medical staff be granted support from management to implement preventative strategies.

Due to the small sample size of this study, no conclusions could be drawn from this study. It is therefore recommended that the study should be repeated with a larger sample size intubated for longer periods as most of the subjects enrolled in this study were not ventilated for long periods. Hopefully a more significant result will then be obtained. According to the researcher the HiLo Evac Lanz^{TM} is one of the ideal types of endotracheal tubes. This type of tube provides both removal of subglottic suctioning and maintaining correct cuff pressure. Unfortunately, this tube has not been sufficiently investigated due to the untimely entry of the confounding variable.

Some preventative measures are well known to healthcare providers, but are not always adhered to. Future studies should be preformed to determine the hindrances in the prevention of ventilator-associated pneumonia. There may be financial limitations, lack of knowledge, lack of skills, lack of staff to perform skills, unwillingness to learn new procedures etc.

8.5. CONCLUSIONS

The prevention of ventilator-associated pneumonia still remains a challenge for the critical care nurse. The last word has not been spoken regarding the solution to this problem. Ventilator-associated pneumonia can be prevented by using non-invasive methods of ventilation, if not possible by limiting the time of intubation together with utilizing evidence-base strategies to prevent ventilator-associated pneumonia. Nursing staff should be educated regarding preventatives strategies and should get involve with research regarding these challenges.

REFERENCES

ALBERT, A. SPIRO, S. & JETT, J. 1999. ***Comprehensive Respiratory Medicine***. London: Mosby.

AMERICAN THORACIC SOCIETY. 1996. Hospital-acquired Pneumonia in Adults: Diagnosis, Assessment of Severity, Initial Antimicrobial Therapy, and Prevention Strategies. ***American Journal of Critical Care Medicine***, 153:1711-1725.

BARAIBAR, J. CORREA, H. MARISCAL, D. GALLEGO, M. VALLéS, J. & RELLO, J. 1997. Risk factors for infection by *Acinetobacter baumannii* in intubated patients with nosocomial pneumonia. ***Clinical Investigations in Critical Care,*** 112(4): 1050-1054.

BOCHICCHIO, G. JOSHI, M. BOCHICCHIO, K. TRACY, K. & SCALEAT. 2004. A Time Dependent Analysis of Intensive Care Unit Pneumonia in Trauma Patients. ***The Journal of Trauma, Injury and Critical Care*** [online], 56(2). Available from:< http:// www.jtrauma.com/pt/re/jtrama/abstract.00005373-2004020000-00010.ht.;jsession…> [Accessed 12/11/2003. 15:35].

BOGGS, R.L. & WOODRIDGE – KING, M. 1993. ***AACN Procedure Manual for Critical Care.*** 3rd Edition. Philadelphia: Saunders.

BORTON, D. 1996. WBC Count and Differential. ***Nursing 96***, 26(9):26-31.

BOWTON, D.L. 1999. Nosocomial Pneumonia in the ICU-Year 2000 and Beyond. ***Chest***, 115(3): 28S-32S.

BRINK, H.I. 1996. ***Fundamentals of Research Methodology for Health Care Professionals***. 2nd Edition. Cape Town: Juta & Company.

BURNS, N. & GROVE, S.K. 1997. ***The practice of nursing research***. 3rd Edition. Philadelphia: Saunders.

CENTERS FOR DISEASE CONTROL AND PREVENTION. 1997. ***Issues in the Healthcare Setting*** [online]. Division of Health Care Quality Promotion. Available from:<*http://www.cdc.gov./ncidod/hip/ISOLAT/iso.htm>[Accessed* 16 September 2003. 14:15].

CHASTRE, J. TROUILLET, J.L. VUAGNAT, A. JOLY-GUILLOU, M.L. CLAVIER, H. DOMBERT, M.C. & GIBERT, C. 1998. Nosocomial Pneumonia in Patients with Acute Respiratory Distress Syndrome. ***American Journal of Critical Care Medicine***, 157:1165-1172.

CLARK, J.M. & HOCKEY, L. 1989. ***Further research for nursing***. Middlesex: Scutari Press.

COOK, D. JONGHE, B. BROCHARD, L. & BRUN-BUISSON, C. 1998. Influence of Airway Management on Ventilator-Associated Pneumonia. ***JAMA***, 279(10): 781-787.

CRAVEN, D.E. LICHTENBERG, D.A. GOULARTE, T.A. MAKE, B.J. & MCCABE, W.R. 1985. Contaminated Medication Nebulizers in Mechanical Ventilator Circuits. ***The American Journal of Medicine***, 77: 834-838.

CRAVEN, D.E. & STEGER, K.A. 1995. Epidemiology of Nosocomial Pneumonia: New Perspectives on an Old Disease. ***Chest***, 108(2):1S-16S.

CRIMLISK, J.T. HORN, M.H. WILSON, D.J. & MARINO, B. 1996. Artificial airways: A survey of cuff management practices. ***Heart & Lung,*** 25(3): 225-235.

DERISO, A.J. LADOWSKI, J.S. DILLON, T.A. JUSTICE, J.W. & PETERSON, A.C. 1996. Chlorhexidine Gluconate 0.12% Oral rinse Reduces the Incidence of Total Nosocomial Respiratory Infection in Nonprophylactic Systemic Antibiotic Use in Patients Undergoing Heart Surgery. ***Chest***, 109(6):1556-1561.

DEPPE, S.A. KELLY, J.W. THOI, L.L. CHUDY, J.H. LONGFIELD, R.N. DUCEY, J.P. TRUWIT, C.L. & ANTOPOL, M.R. 1990. incidence of colonization, nosocomial pneumonia, and mortality in critically ill patients using a Trach Care™ closed- suction system versus an open-suction system: Prospective, randomised study. ***Critical Care Medicine***, 18(12): 1389-1394.

EGGIMANN, F. & PITTET, D. 2001. Infection Control in the ICU. ***Chest***, 120(6): 2059-2093.

ELLSTROM, K.E. 1999. Breathing easier in the Intensive Care Unit. ***Critical Care Nursing Clinics of North America***, 11(4): 409-421.

FARMOVS PAREXEL, 2000. ***Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa***. Bloemfontein: Department of Health.

FINK, J.B. KRAUSE, S.A. BARRET, L. SCHAAFF, D. & ALEX, C.G. 1998. Extended Ventilator Circuit Change Interval Beyond 2 Days Reduces the Likelihood of Ventilator-Associated Pneumonia. ***Chest,*** 113(2):405-411.

FOURRIER, F. DUVIVIER, B. BOUTIGNY, H. ROUSSEL-DELVALLEZ, M. & CHOPIN, C. 1998. Colonization of dental plaque: A source of nosocomial infections in intensive care unit patients. ***Critical Care Medicine***, 26(2): 301-308.

FRISANCHO, A.R. 1999. ***Anthropometric Standards for the Assessment of Growth and Nutritional Status.*** 4th Edition. United States of America: University of Michigan.

GIBBON, C.J & SWANEPOEL, C.R. 1995. ***South African Medicines Formulary***. 3rd Edition. Medical Association of South Africa: Cape Town.

GIROU, E. STEPHAN, F. NOVARA, A. SAFAR, M. & FAGON, J. 1998. Risk Factors and Outcome of Nosocomial Infections: Results of a Matched Case-control Study of ICU Patients. ***American Journal of Respiratory Critical Care Medicine****,* 157:1151-1158.

GRAP, M.J. & MUNRO, C.L. 1997. Ventilator associated-pneumonia: Clinical significance and implications for nursing. ***Heart & Lung***, 26(6): 419-429.

GRAP, M.J. & MUNRO, C.L. ASHTIANI, B. & BRYANT, S. 2003. Oral care interventions in critical care: frequency and documentation – a survey of oral care practices for reducing dental plaque, oral colonization, and ventilator-associated pneumonia in critical ill patients. ***American Journal of Critical Care***, 12:113-119.

GUYTON, D.C. BARLOW, M.R. & BESSELIEVRE, T.R. 1997. Influence of airway pressure on minimum occlusive endotracheal tube cuff pressure. ***Critical Care Medicine****,* 25(1): 91-94.

HARRIS, J.R. & MILLER, T.H. 2000. Preventing Nosocomial Pneumonia: Evidence-Based Practice. ***Critical Care Nurse***, 20(1): 51-65.

HICKEY, J.V. 1997. ***The clinical Practice of Neurological and Neurosurgical Nursing***. 4th Edition. Philadelphia: Lippincott.

HODGE, M. KOCHIE, L.D. LARSON, L. & SANTIAGO, M. 2003. Clinician-implemented research utilization in critical care - CE Online. ***American Journal of Critical Care*** [online], 12(4). Available from:< http://www.findarticles. com/p/articles/mi_m0NUB/is_4-12/ai_105556279.> [Accessed 29 September 2004].

ICH GUIDELINES. 2002. ***Selected ICH Guidelines and the Declaration of Helsinki.*** Philadelphia: Clinical Research Resources.

JOHNSON, K.L. KEARNEY, P.A. JOHNSON, S.B. NIBLETT, J.B. MacMILLAN, N.L. & McCLAIN, R.E. 1994. Closed versus open endotracheal suctioning: Cost and physiological consequences. ***Critical Care Medicine****.* 22(4): 658-665.

JOUBERT, G. BAM, R.H. & CRONJE, H.S. 1999. ***How to write a protocol: a manual for beginner researchers****.* Bloemfontein: Department of Biostatistics and department of obstetrics and gynecology.

KITE, K. & PEARSON, L. 1995. A rationale for mouth care: the integration of theory with practice. ***Intensive and Critical Care Nursing****,* 11:71-76.

KOLLEF, M.J. 1999. The prevention of ventilator associated pneumonia. ***New England Journal*****,** 340(8): 627-633.

KOLLEF, M.F. SKUBAS, N.J. & SUNDT, T.M. 1999. A Randomized Clinical Trial of Continuous Aspiration of Subglottic Secretions in Cardiac Surgery Patients ***Chest***, 116(5): 1339-1346.

KOLLEF, M.H. PRENTICE, D.P. SHAPIRO, S.D. FRASER, V.J. SILVER, P. TROVILLION, E. WEILITZ, P. VON HARTZ, B. & ST. JOHN, R. 1997. Mechanical Ventilators with or without Daily Changes of In-line Suction Catheters. ***American Journal of Respiratory Critical Care Medicine***, 156:466-472.

LEE, R.D. & NIEMAN, D.C. 1993. ***Nutritional Assessment***. Iowa: Brown.

LUNA, C.M. VIDELA, A. MATTERA, J. VAY, C. FAMIGLIETTI, A. VUJACICH, P. & NIEDERMAN, M.S. 1999. Blood cultures have limited value in predicting severity of illness and as a diagnostic tool in ventilator-associated pneumonia.

Chest, 116(4):1075-1085.

LYNCH, J.P.III. 2001. Hospital-Acquired Pneumonia: Risk Factors, Microbiology, and Treatment. ***Chest***, 119(2): 373S-384S.

MAHAN, L.K. 1996. ***Krause's Food, Nutrition and Diet Therapy***. 9th Edition. Philadelphia: WB Saunders Company.

MAHONEY, F.I. & BARTHEL, D. 2002. ***Barthel index*** [online] Yale-New Haven Hospital. Available from: <**http://www.info.med.yale.edu/neurol/residency/barthel.hjml**> [Accessed: 11 June 2002. 10:20].

MAHUL, P. AUBOYER, C. JOSPE, R. ROS, A. GUERIN, C. EL KHOURI, Z. GALLIEZ, M. DUMONT, A. & GADIN, O. 1992. Prevention of nosocomial pneumonia in intubated patients: respective role of mechanical subglottic secretions drainage and stress ulcer prophylaxis. ***Intensive Care Medicine,*** 18:20-25.

MALHOTRA, N.K. 2002. ***Basic Marketing Research: Applications to Contemporary Issues***. Prentice Hall: New Jersey.

MALLINCKRODT MEDICAL. 2000. ***Cairways: Intensove Care Tracheal Tubes***. Oxfordshire:Mallinckrodt Inc.

MALLINCKRODT MEDICAL. 2000. ***Hi-Lo Lanz ™ , HiLo ™ Evac, HiLo Evac/Lanz™, Satin Soft HiLo Lanz ™***. St. Louis:Mallinckrodt Inc.

MALLINCKRODT MEDICAL. 2002. ***HiLo ™ Evac, HiLo Evac/Lanz™: From bottom to top- Evac works***. United Kingdom: Mallinckrodt Medical Ltd.

MATHEWS, P.J. & MATHEWS, M. 2000. Reducing the risk of ventilator-

associated pneumonia infections. ***Dimensions of Critical Care Nursing***, 19(1): 17-21.

MAYHALL, C.G. 2001. Ventilator-Associated Pneumonia or Not? Contemporary Diagnosis. ***Emerging Infectious Diseases***, 7(2): 200-204.

MEDURI, G.U. MAULADIN, G.L. WUNDRINK, R.G. LEEPER, K.V. JONES, C.B. TOLLEY, E. & MARSHALL, G. 1994. Causes of Fever and Pulmonary Densities in Patients with Clinical Manifestations of Ventilator-Associated Pneumonia. ***Chest***, 106(1): 221-235.

MILLER, B.F. & KEANE, C. B. 1978. Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health. 2nd Edition. Philadelphia: W.B. Saunders Company.

MOL, D.A. DE VILLIERS, G. DU T. CLAASEN, A.J. & JOUBERT, G. 2003. ***The use and care of an endotracheal / tracheostomy tube cuff-are intensive care unit staff adequately informed?*** Thesis M.Med. Bloemfontein: University of the Free State.

MULDER, M. SMALL, N. BOTMA, Y. ZIADY,L. & MACKENZIE, J. 2002. **Basic Principles of Wound Care.** Cape Town:Pearson Education South Africa.

MUNRO, C.L. & GRAP, M.J. 2001. Nurses' knowledge and attitude about antibiotic therapy in critical care. ***Intensive and Critical Care Nursing***,17:213-216.

NAIKOBA, S. & HAYWARD, A. 2001. The effectiveness of interventions aimed at increasing handwashing in healthcare workers-systematic review. ***Journal of Hospital Infection***, 47:173-180.

OIKKONEN, M. & AROMAA, U. 1997. Leakage of fluid around low-pressure tracheal tube cuffs. ***Anaesthesia,*** 52:567-569.

OROZCO-LEVI, M. TORRES, A. FERRER, M. PIERA, C. EL-EBIARY, M. DE LA BELLACASA , J.P. & RODRIGUES-ROISIN, R. 1995. Semirecumbent Position Protects from Pulmonary Aspiration but not Completely from Gastroesphageal Reflux in Mechanically Ventilated Patients. ***American Journal of Respiratory Critical Care Medicine***, 152:1387-1390.

QUIRKE, S. & FRENCH, K. 1996. Changing ventilator tubing circuits every seven days versus every 72 hours: proposed practice based on literature review. ***Intensive and Critical Care Nursing****,* 12:277-279.

REESE, R.E. & BETTS, R.F. 1996 ***. A practical approach to infectious diseases***. 4th Edition. Boston: Little Brown and Company.

RELLO, J. RUÉ, M. JUBERT, P. MUSES, G. SONORA, R. VALLÉS, J. & NIEDERMAN, M.S. 1997. Survival in patients with nosocomial pneumonia: Impact of the severity of illness and etiologic agent. ***Critical Care Medicine***, 25(11): 1862-1866.

RELLO, J. SONORA, R. JUBERT, P. ARTIGAS, A. RUÉ, M. & VALLéS, J. 1996. Pneumonia in Intubated Patients: Role of Respiratory Airway Care. ***American Journal of Respiratory Care Medicine***, 154: 111-115.

SEEGOBIN, R.D. & VAN HASSELT, G.L. 1986. Aspiration beyond endotracheal cuffs. ***Canadian Anaesthetists' Society Journal***, 33(3):273-279.

SHORR, A.F. & O'MALLEY, P.G. 2001. Continuous Subglottic Suctioning for the prevention of Ventilator-Associated Pneumonia. ***Chest***, 119(1): 228-235.

SMULDERS, K. VAN DER HOEVEN, H.,WEERS-POTHOFF, I. & VANDENBROUCKE-GRAULS, C. 2002. A Randomized Clinical Trial of Intermittent Subglottic Secretion Drainage in Patients Receiving Mechanical Ventilation. ***Chest***, 121(3):858-862.

SOLTÉ, S. BIEDLER, S. SILOMON, M. SCHÖPHFLIN, I. & MOLTER, G.P. 2001: ***Recovery after remifentanil and sufentanil for analgesia and sedation of mechanically ventilated patients after trauma or major surgery***. [online] Available from:http://www.bja.oupjournals.org/cgi/content/full [Accessed 29 September 2004].

SPILKER, B. 1987. ***Guide to Planning and Managing Multiple Clinical Studies***. New York: Raven Press.

SPIKER, B.1991. ***Guide to Clinical Trials***. New York: Raven Press.

TABLAN, O.F. ANDERSON, L.J. BESSER, R. BRIDGES, C. & HAJJEH, R. 2003. ***Guidelines for preventing health care-associated pneumonia.*** [online] Centers for Disease Control and Prevention and Healthcare infection control practices advisory committee. Available from:<http:// www.cdc.gov/ncidod/hip/guide/CDCpneumo-guidelines.pdf> [Accessed 07/07/2004:12:24].

TASOTA, F.J. FISHER, E.M. COULSON, C.F. & HOFFMAN, L.A. 1998. ***Protecting the ICU Patients From Nosocomial Infections: Practical Measures for Favorable Outcomes***. [online] Available from:< http://www.critical-care-nurse.org/aacn/jrn/ccn>[Accessed 08 January 2002. 12:47].

THELAN, L.A. URDEN, L.D. LOUGH, M.E. & STACY, K.M. 1998. ***Critical Care Nursing: Diagnosis and Management***. 3rd Edition. St Louis: Mosby.

THOMACHOT, L. VIALET, R. ARNAUD, S. BARBERON, B. MICHEL-NGUYEN, A. & MARTIN. C. 1999. Do the components of heat and moisture exchange humidifier filters affect their humidifying efficacy and the incidence of nosocomial pneumonia? ***Critical Care Medicine***, 27(5): 923-926.

THOMPSON, C.L. 1995. Critical Care- Acquired Pneumonia. ***Critical Care Nursing Clinics of North America***, 7(4): 695-701.

TORRES, A. GATELL, J.M. AZNAR, E. EL-EBIARY, M. PUIG DE LA BELLACASA, J. GONZÁLLES, J. FERRER, M. & RODRIQUEZ-ROISIN R. 1995. Re-intubation Increases the Risk of Nosocomial Pneumonia in Patients Needing Mechanical Ventilation**.** ***American Journal of Critical Care Medicine***, 152: 137-141.

TUFTS UNIVERSITY. 2000. ***Health and Age***. [online] Available from: http://www. Healthandage.com/Phome/gid2=1038. > [Accessed 12/11/2004. 15:30].

TYCO HEALTHCARE, 2002. ***Closed suction system for adults***. Mallinckrodt Dar; Italy.

UNIVERSITY OF MICHIGAN, 2002. ***Infection control***. [online] Available from: <***http://www.med.umich.edu***. > [Accessed16 September 2003. 15:30].

UYS, H.H.H. & BASSON, A.A. 1995. ***Research Methodology in Nursing***. 2nd Edition. Pretoria: KAGISO Tertiary.

UYS, H.H.H. & BASSON, A.A. 2000. ***Research Methodology in Nursing***. 8th Edition. Cape Town: KAGISO Tertiary.

VALLéS, J. ARTIGAS, A. RELLO, J. BONSOMS, N. FONTANALS, D. BLANCH, L. FRENÁNDES, R. BIAGORRI, F. & MESTRE, J. 1995. Continuous Aspiration of the Subglottic Secretions in Preventing Ventilator- Associated Pneumonia. ***Annals of Internal Medicine***, 122(3): 179-186.

WARE, J.E. & DEWEY, J.E. 2000. ***Health Status and Outcome Assessment Tools***. [online] Available from:<http://www.Iejhe.siu.edu.>[Accessed 11 June 2002. 16:30].

WILLIAMS, J.D. SHARMA, K.B. ATUKORALA, S.D. KELKAR, R. SHARMA, A. WATTANAASRI, S. LOLEKHA, S. & UNAHALEKHAKA, A. 2002. ***Guidelines on Prevention and Control of Hospital Associated Infections****.* New Dehli: World Health Organization.

WOOD, C.J. 1998. Endotracheal suctioning a literature review. ***Intensive and Critical Care Nursing***, 16:124-136.

WUNDERINK, R.G. 1999. Prevention of ventilator-associated pneumonia. ***Chest***, 116(5): 1155-1156.

YOUNG, P.J. BASSON, C. HAMILTON, D. & RIDLEY, S.A. 1999. Prevention of tracheal aspiration using the pressure-limited tracheal tube cuff. ***Anaesthesia***, 54:559-563.

YOUNG, P.J. & RIDLEY, S.A. 1999. Ventilator-associated pneumonia: Diagnosis and prevention. ***Anaesthesia***, 54:1183-1197.

ADDENDUM 1

STANDARD OPERATING PROCEDURE

STANDARD OPERATING PROCEDURE

THE EFFECT OF THREE TYPES OF ENDOTRACHEAL TUBES ON VENTILATOR-ASSOCIATED PNEUMONIA

RESEARCHER
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Tel: 082 954 6122

CHAPTER 1
DESCRIPTION OF RESEARCH

1.1. Introduction

The standard operating manual has been compiled as a reference for those involved with the research. Chapter 1 addresses the general concepts of the research. The chapters that follow are divided to address each group involved. In case of any problems, first consult Chapter 1 and then the specific chapter that you are involved with. Please contact the researcher when problems are experienced or in case of any questions (telephone number available on cover of Standard Operating Manual). Your participation in this research is sincerely appreciated.

The research implementation is summarized in Figure 1.

1.2. Aim and Objectives of the research

The aim of the research is to determine the effect of three types of endotracheal tubes on ventilator-associated pneumonia. The research **objectives** are to compare three groups of subjects, intubated with different types of endotracheal tubes regarding the:

a) incidence of ventilator-associated pneumonia;
b) risk factors;
c) causative organisms;
d) length of intensive care stay;
d) cuff pressures;
e) morbidity; and
f) mortality.

1.3. Population group of the research

The population is all candidates that are admitted to the Neurosurgical Intensive Care Unit of a public Hospital in Bloemfontein, who are intubated before neurosurgery in theatre, or in the Neurosurgical Intensive Care Unit and who meet the criteria of the study.

1.4. Inclusion and exclusion criteria of the research

The researcher will screen the subjects regarding inclusion and exclusion criteria of the research as listed below.

1.4.1. Inclusion criteria

Candidates will be included in the study if they are:

a) 18 years and older; and
b) expected to be intubated and ventilated longer than 48 hours.

1.4.2. Exclusion criteria

Candidates will be excluded from the study if they:

a) have a neutrophyl count of less than 1.6 X 10^9 /l (NHLS Laboratories values);
b) have a lymphocyte count of less than 0.6 X 10^9 /l ;
c) have experienced aspiration before or during intubation;
d) are diagnosed with a pneumonia before intubation;
e) are expected to be ventilated for less than 48 hours;
f) used antibiotics at the onset of the study;
g) are intubated in another hospital, ward or intensive care unit than at the research site;
h) are diagnosed with primary lung cancer or other lung metastases;
i) are subjects in a clinical trail of a drug or device within 30 days prior to entering the trial;
j) are diagnosed with cystic fibrosis; or
k) are diagnosed with or suspected of having tuberculosis.

The identification of candidates is done by the Neurosurgeon and is crucial as the population group is limited. The procedure of notifying the researcher regarding candidates is explained in 3.2.

1.5. TRAINING OF RELEVANT PARTIES

The researcher will assign each subject to a specific study group. The researcher will train the anaesthetist, anaesthesia nurse, nursing and physiotherapy staff of the Neurosurgical Intensive Care Unit, in the management of the endotracheal tubes. The nursing staff and the physiotherapist will perform these procedures according the Standard Operating Procedure Manual. (See Chapter 4. GUIDELINES FOR NURSING STAFF AND PHYSIOTHERAPISTS.) See Figure 1 for the Flow Diagram of the research.

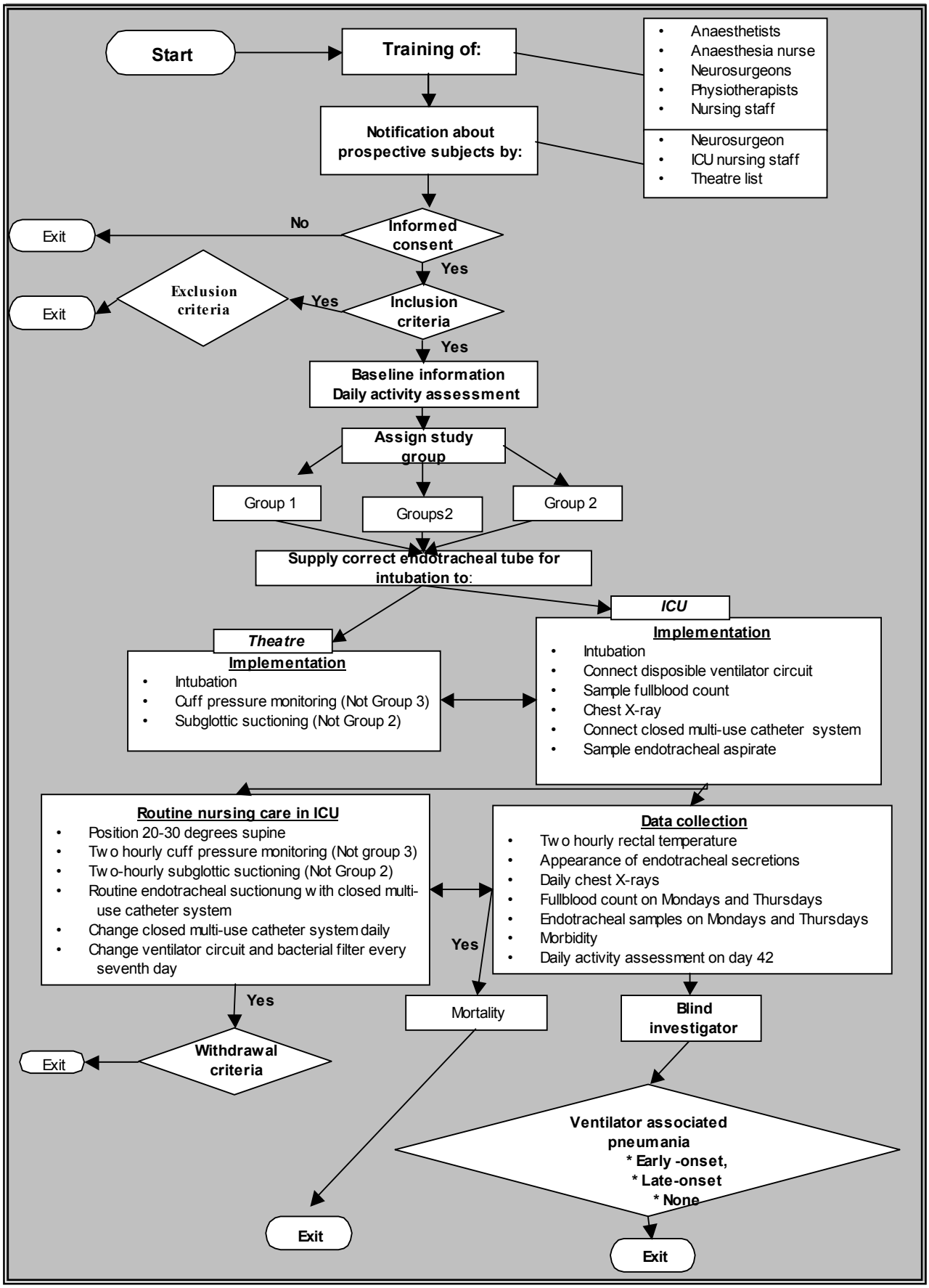

Figure 1: Flow diagram of research implementation

1.6. Description of the three types of endotracheal tubes

The three types of endotracheal tubes to be used in the study are: Hi-Contour ™ (*Mallinckrodt, Athlone, Ireland*), HiLo ™ Evac (*Mallinckrodt, Athlone, Ireland*) and HiLo Evac Lanz ™ (*Mallinckrodt, Athlone, Ireland*).

The **Hi-Contour ™** (*Mallinckrodt, Athlone, Ireland*) tube used, conventionally, does not facilitate subglottic suctioning (see figure 2). Cuff measurements should be preformed two hourly and maintained between 25 and 33 cmH_2O.

Figure 2: Hi-Contour endotracheal tube (Mallinckrodt: 2000:4)

The **HiLo ™ Evac** (*Mallinckrodt, Athlone, Ireland*) allows for subglottic suctioning (see figure 3). The cuff pressure should also be managed as mentioned above. Subglottic suctioning performed every two hours.

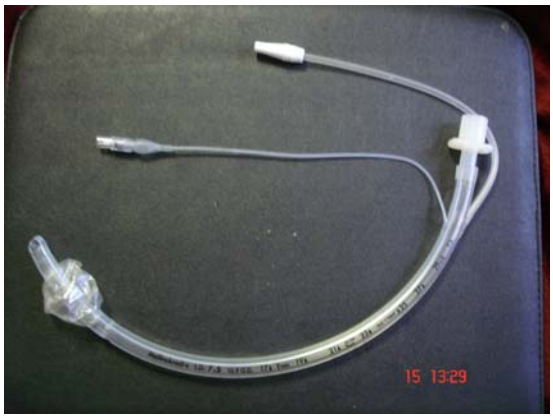

Figure 3: HiLo ™ Evac endotracheal tube

The **HiLo Evac Lanz ™** (*Mallinckrodt, Athlone, Ireland*) has a Lanz ™ valve which maintains the cuff pressure automatically (see figure 4). After intubation the Lanz ™ valve should be inflated with 40 ml of air. Cuff pressure monitoring is not necessary in this type of endotracheal tube as the Lanz™ valve automatically regulates the pressure between 30 and 34 cm H_2O. When properly inflated, the balloon will fill 2/3 of the protective cover. THE MANUFACTURER ADVICE IS NOT TO SQUEEZE THE BALLOON.

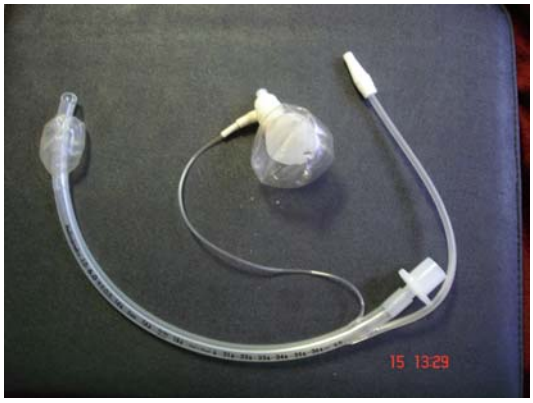

Figure 4: Hi-Lo Evac Lanz ™ endotracheal tube

It is important at all times are adhered to the following infection control principles:

- Wash your hands before and after touching the subject.
- Adhere to aseptic techniques when performing all procedures.
- Adhere to universal infection control principles.

1.7. SPECIFICATIONS AND DESCRIPTIONS OF DEVICES USED IN RESEARCH

Below is a thorough description of the endotracheal tubes used during the research. The other devices used in this research are: a calliper (used for anthropometric measurements), a cuff pressure monitor, closed multi-use catheter systems, inspiratory and expiratory bacterial filters, disposable ventilator circuits and disposable rectal thermometers.

1.7.1. Types of endotracheal tubes

The types of endotracheal tubes, which will be used in this research, are the following:

1. The Hi-Contour ™ *(Mallinckrodt, Athlone, Ireland) endotracheal tube*
2. The HiLo™ Evac *(Mallinckrodt, Athlone, Ireland) endotracheal tubes*
3. The HiLo Evac Lanz ™ valve (Mallincrodt, Athlone, Ireland) endotracheal tubes.

1.7.1.1. Common features of the HiLo™ Evac and the HiLo Evac Lanz™ valve endotracheal tube

Below is mentioned the characteristics of the endotracheal tubes used in the research.

Clear tube material
It allows for visualization of condensed exhaled air indicating tracheal intubation.

Thermosensitive material
The clear thermosensitive material softens at body temperature to follow the natural airway profile and minimizes the possibility of damage to the tracheal mucosa.

Thin walled tube
This ensures a large internal diameter in comparison to the external diameter. This allows a wider choice of tube size without compromising the airflow resistance.

Atraumatic tip
The rounded tip reduces the risk of tracheal wall damage during intubation.

Pilot balloon with self-sealing valve
The inflation line is a self-sealing valve and pilot balloon.

Magill shaped body
The body of the tube is curved through to the distal tip conforming to ISO & EN criteria.

Standard connector
The endotracheal tube is fitted with a standard connector to secure the breathing system. The internal shoulder is tapered for easy passage of suction catheters. The tracheal tube size is marked on the connector.

Sterile packed
The fact that the tubes are sterile packed reduce the risk of infection.

Latex free
The endotracheal tube is made of material that is latex free.

CE approved
These endotracheal tubes are CE approved in accordance with Council Directive 93/94/EEC of 14th June 1993.

Subglottic suctioning
Both endotracheal tubes has an additional lumen into the wall of the endotracheal tube, when connected to a suctioning device, allows for removal of secretions from the subglottic space.

X-ray opaque marker
This marker allows for conformation of the position of the endotracheal tube after intubation.

1.7.1.2. The HiLo cuff criteria of the HiLo^{TM} Evac and the HiLo Evac Lanz^{TM} valve endotracheal tube

Thin-walled cuff (0,05mm)
The cuff conforms to the uneven surfaces of the trachea to create a low-pressure seal to minimize the risk of micro-aspiration.

Resting diameter (one and a half times the average trachea diameter)
This size is required recommended to achieve a low-pressure seal. To a slight degree, the trachea expands and contracts due to airway pressure changes. A cuff must be able to expand and contract with the trachea and still maintain this low-pressure seal.

Large resting volume
The long cuff length and large resting volume is required to ensure that the intra-cuff pressure is distributed over a larger surface area of the tracheal wall. In combination, these two factors help to achieve a low-pressure seal in the tracheal to provide a better aspiration protection to the lower airways.

High compliance
The cuff compliance relates to the elasticity and softness of the cuff. The fact that the cuff is so elastic and soft allows for easy visualisation of the vocal cords during intubation.

Low intra-cuff pressure
Low–pressure cuffs reduce the risk of damage to the tracheal wall tissue.

1.7.1.3. Specifications of the endotracheal tubes

The different types of endotracheal tubes to be used in the research are listed in Table 1.

Table 1: Specifications of the research endotracheal tube

Type of endotracheal tube	Endotra-cheal tube size	Inner diameter (mm)	Outer diameter (mm)	Cuff resting diameter (mm)	Length (mm)
Hi-Contour™	7.5	7.5	10.2	26	350
	8.0	8.0	10.9	30	360
	8.5	8.5	11.5	32	370
HiLo™ Evac	7.5	7.5	10.3	32	375
	8.0	8.0	11.5	33	376
	8.5	8.5	12.2	34	376
HiLo Evac Lanz™	7.5	7.5	10.2	30	350
	8.0	8.0	10.9	33	360
	8.5	8.5	11.5	34.	370

1.7.1.4. Lanz™ system of the HiLo Evac Lanz™ endotracheal tube

The benefit of the Lanz™ System is the following:

BENEFITS

1. The Lanz™ System automatically controls and limits cuff pressure, therefore preventing over-inflation.
2. The large external balloon allows for simple visualization of the functional state of the cuff.
3. Reduces the risk of silent aspiration
4. Provides a safe seal if the initial inflation is between 20ml to 45ml of air to maintain intra-cuff pressure between 30 to 34 cmH_2O
5. The Lanz™ valve is an integral part of the endotracheal tube, which prevents disconnection from the endotracheal tube.

1.7.2. Management of all endotracheal tubes and other devices

The management of the endotracheal tubes and other devices should be managed in the following manner:

1.7.2.1. Supply, storage and dispensing

The endotracheal tubes are stored in an area with limited access, namely the office of the principle investigator, which is kept locked at al times. The endotracheal tubes will be kept at room temperature of 21-24 ^{0} C. Before surgery, three sizes 7.5, 8.0 and 8.5 will be handed over to the sister of anaesthesia. After intubation the tubes not used will be collected from theatre and stored.

1.7.2.2. Inventory

The principle investigator will ensure records of endotracheal tubes received from the sponsor. Records will be kept of the endotracheal tubes issued to the

anaesthesia nurse or returned by her. The size of the endotracheal tube used during intubation will be recorded on the patient's research number.

1.7.3. Devices used in research

In Table 2 is listed the other devices utilized during the research. Contact the researcher if any problems are experienced or if you are unfamiliar with the devices.

Table 2: List of devises utilized in research

Instrument	Product	Supplies provided by Sponsor
Calliper	Lord Bull	
Cuff pressure monitor	Hi-Lo™ Hand Pressure Gauge	Tyco Health Care (*Mallinckrodt*)
Closed multi-use catheter system	Dar Ty-Care Closed System for Tracheo-bronchial suction	Tyco Health Care (*Mallinckrodt*)
Inspiratory bacterial filter (Bacterial filter for mechanical ventilation in intensive care unit)	Sterivent S -Mechanical Breathing filter	Tyco Health Care (*Mallinckrodt*)
Inspiratory bacterial filter (Bacterial filter for use during theatre period of ventilation)	Dar Hygrobac, "S" Filter/HME	Tyco Health Care (*Mallinckrodt*)
Disposable ventilator circuit	Dar Embedded Heater-Wire Intensive Care Breathing Circuit	Tyco Health Care (*Mallinckrodt*)
Humidifier	Fisher and Packel Humidifier	
Disposable rectal probe	Mono-a-therm™	Tyco Health Care (*Mallinckrodt*)
Cable for disposable rectal probe	Mon-a-therm ® Temperature System Instrument cable	Tyco Health Care (*Mallinckrodt*)
Rigid suction tip for mouth care	Argyle Yankauer suction instrument	Tyco Health Care (*Mallinckrodt*)

CHAPTER 2
GUIDELINES FOR THE ANAESTHETISTS AND ANAESTHESIA NURSES

2.1. INTRODUCTION

The anaesthetist is responsible for the intubation of the subjects enrolled into this research. Before surgery, the researcher will provide the correct type of endotracheal tube in three sizes namely: 7.5, 8.0 and 8.5. The researcher decides which type of endotracheal tube will be use for intubation. The anaesthetist determines the size of the endotracheal tube suitable for the patient.

2.2. GENERAL GUIDELINES DURING INTUBATION

- Only the anaesthetist is allowed to intubate the subject (This is to limit the variables in the research).
- Check the endotracheal cuff for any leaks before intubation by inflating the cuff.
- Sterile intubation techniques like: intubation from a sterile intubation tray, maintaining sterility of the endotracheal tube etc., should be adhered to during intubation.
- Do not apply too much lubricant to the endotracheal tube. Excessive amounts of lubricant may lead to drying out of the inner wall of the trachea. This may lead in turn to a phlegm plug and to partial or complete airway obstruction. (Mallinckrodt, 2000:2)
- Aspiration of gastric content should be prevented at all times during intubation. Suspected aspiration should be indicated on the An*aesthesia Report* form.
- After intubation, the endotracheal tube should be secured to prevent movement or extubation during surgery, while transferring of the subject to the bed or changing of subject's position.
- Wash hands before and after touching the subject.
- Adhere to aseptic techniques during all procedures performed on the patient.

2.3. Measuring the cuff pressure in case of the Hi-contour^{tm} and hilo ^{TM} Evac

Cuff pressure should be monitored after intubation and every two hours. This will prevent both leaking of secretions past the cuff and over-inflation.

2.3.1. Procedure

1. Connect the cuff manometer line to the inflation valve of the endotracheal tube after intubation and inflation of the cuff.
2. Measure the cuff pressure.
3. If cuff pressure is less than 25 cmH_2O inflate the cuff with the manometer until the correct cuff pressure is reached.
4. If the pressure is higher than 33 cm H_2O, open the release valve on the

left side of the manometer until correct pressure is reached.

5. Perform this procedure every 2 hours and record cuff pressure on Anaesthesia Report form.

The cuff monitor should remain connected to valve inlet as air escapes with every connection and disconnection.

2.4. SUBGLOTTIC SUCTIONING PROCEDURE IN CASE OF THE HILO ™ EVAC AND HILO EVAC LANZ ™

Subglottic suctioning is a procedure that removes subglottic secretions from the orofarynx and prevents aspiration past the endotracheal tube cuff.

2.4.1. Procedure

1. Subglottic suctioning should be preformed every two hours or more frequently during surgery.
2. Connect the subglottic suctioning outlet to the suction tubing of a Gabler suction device.
3. Open the Gabler suction device and apply suctioning at a negative pressure of 100mg Hg for 8 seconds. Close the suction device for 20 seconds until no further secretions are aspirated.
4. If blockage of the Evac lumen is suspected, it may be cleared by injecting 1 ml of **air** through the lumen to maintain patency.
5. Record the performance of subglottic suctioning on the *Anaesthesia Report and Intubation* forms (Table 3).

TABLE 3: ANAESTHESIA REPORT FORM

For official use

Hospital Number

Study number

1-2

DATE

Day	Month	Year

d d m m y y

3-8

Time of intubation

		:		

End of anaesthesia

		:		

Initial and Surname of Anaesthetist

_____

1. Subglottic suctioning and cuff pressure monitoring (Performed by the Anaesthetist)

Subglottic suctioning (√ when procedure has been performed)		**Endotracheal cuff pressure** (Maintained between 25-33cm H_2O)
Time	**Performed**	**Pressure**
02:00		
04:00		
06:00		
08:00		
10:00		
12:00		
14:00		
16:00		
18:00		
20:00		
22:00		
24:00		

	9		10-11
	12		13-14
	15		16-17
	18		19-20
	21		22-23
	24		25-26
	27		28-29
	30		31-32
	33		34-35
	36		37-38
	39		40-41
	42		43-44

2. Aspiration during intubation suspected?

Y	**N**
1	2

45

3. Position during surgery

Supine	**Prone**
1	**2**

46

3. Duration of anaesthesia

Hours		**Minutes**	

		:		

47-51

CHAPTER 3
GUIDELINES FOR THE NEUROSURGEONS

3.1. INTRODUCTION

The role of the neurosurgeon in this research is two-fold. Firstly, the neurosurgeon assists with the identification by reporting prospective candidates. The procedure will be explained below.

Secondly, in some circumstances prospective candidates may require intubation in Neurosurgical Intensive Care unit. The correct type of endotracheal tubes will be available on the emergency trolley in a marked box in three sizes namely: 7.5, 8.0 and 8.5. The researcher decides which type of endotracheal tube will be used for intubation. The neurosurgeon determines the size of the endotracheal tube suitable for the patient.

After intubation, the Intubation form must be completed, see table 5. This form will be available in the Nurse in charge's office.

3.2. Procedure of notification of the researcher

Notification of the researcher may be performed via two methods, namely written or telephonic.

3.2.1. Written notification

The neurosurgeon will notify the researcher of prospective subjects (see 1.4.1 and 1.4.2 for *Inclusion and Exclusion criteria* respectively) by completing the notification form (see Table 4 below) and folding it in half. This form is available on the notice board outside the ICU Training and Development office next to the Neurosurgical Intensive Care Unit. The form is then posted under the office door.

3.2.2. Telephonic notification

When the neurosurgeon phones the researcher, the researcher completes the form herself with the information provided by the neurosurgeon.

Table 4: Notification form

NOTIFICATION FORM

Prospective subject for research on the effect of three endotracheal tubes on ventilator-associated pneumonia

NAME OF PATIENT: _____

Date: _____

WARD: _____

ROOM NUMBER: _____

NEUROSURGEON: _____

DIAGNOSIS: _____

PROSPECTIVE DATE OF SURGERY: _____

Will the patient be ventilated for more than 48 hours post operatively?
Y / N

Is the patient presently on antibiotic therapy for pneumonia?
Y / N

Has a chest X-ray been taken
Y / N

Has a full blood count been taken
Y / N

Please fold this form in half.

Post the form underneath the Training and Development office door

Researcher: M. Phillips **Tel: 051x 405 3572 or 082 954 6122**

3.3. General guidelines for intubation of subjects in the Neurosurgical intensive care unit

In case of intubation in the Neurosurgical Intensive Care Unit the following guidelines should be followed. Use the endotracheal tube available in the marked box on the emergency trolley. After intubation complete the Intubation form (see Table 5).

- Only the neurosurgeon is allowed to intubate the subject (This is to limit the variables in the research).
- Check the endotracheal cuff for any leaks before intubation by inflating the cuff.
- Sterile intubation techniques like: intubation from a sterile intubation tray, maintaining sterility of the endotracheal tube etc., should be adhered to during intubation.
- Do not apply too much lubricant to the endotracheal tube. Excessive amounts of lubricant may lead to drying out of the inner wall of the trachea. This may lead in turn to a phlegm plug and to partial or complete airway obstruction. (Mallinckrodt, 2000:2)
- Aspiration of gastric content should be prevented at all times during intubation. Suspected aspiration should be indicated on the *Intubation* form.
- After intubation, the endotracheal tube should be secured to prevent movement or extubation during surgery, transferring of the subject to the bed, or changing of subject's position.
- Wash hands before and after touching the subject.
- Adhere to aseptic techniques during all procedures performed on the patient.

Table 5: Intubation form

Hospital Number

Date

Day	Month	Year

Time of intubation

		:		

1. Initial and surname of physician

_____

2. Aspiration during intubation suspected?

Y	N
1	2

3. Route of intubation

Mouth	Nose
1	2

4. Intubation in:

Intensive care unit	Ward
1	2

For official use
Study number

1-2

d d m m y y

3-8

		:		

9-13

14-15

16

17

18

3.4. Blind investigator

A blind investigator will make the diagnosis of a ventilator-associated pneumonia. The researcher will provide the blind investigator with information to make the diagnosis of a ventilator-associated pneumonia. The blind investigator may phone the Neurosurgeon to obtain information about the clinical picture of the patient, if necessary. The blind investigator may not see or examine the patient.

If the patients develop pneumonia, they receive the standard medical and nursing care. (The neurosurgeon does not have to wait for the diagnosis of the blind investigator). The Neurosurgeon prescribes the antibiotic according to the guidelines drawn up by the blind investigator (Table 6). If it necessary to prescribe another antibiotic, this should be first discussed it with the blind investigator.

If an empirical treatment of pneumonia has to be prescribed, it should be discussed with the blind investigator (see Guidelines for the management of ventilator-associated pneumonia 3.4.1).

If the patient develops another nosocomial infection e.g. urinary tract infection, the neurosurgeon treats this according to his own discretion.

The following section has been compiled by Dr J.G.H. Lups as guidelines for the diagnosis of ventilator associated pneumonia and the administration of antimicrobial drugs.

3.4.1. Guidelines for management of ventilator-associated pneumonia

3.4.1.1. Study title

The effects of three types of endotracheal tubes on ventilator-associated pneumonia

3.4.1.2. Objective:

To establish guidelines for the prescription of antibiotics for subjects of the study, in case of a ventilator-associated pneumonia.

3.4.1.3. Definitions

The definitions related to the research are as follows.

Ventilator-associated Pneumonia (VAP)

- As defined in the study protocol

Early Onset VAP

- If present in a patient on mechanical ventilation within 48 to 72 hours after intubation

Late Onset VAP

- VAP that develop 72 hours after intubation

Severe Pneumonia

- Respiratory rate > 30 breaths/min
- Low blood pressure
  Systolic < 90 mmHg
  Diastolic < 60 mmHg
  Need for vasopressors > 4 hours
- Multilobar consolidation
- Extrahoracic septic complications
- Confusion or decreased consciousness

Patients at risk for developing VAP

- Older than 60 years of age
- Chronic lung disease or systemic disease
- Recent antibiotic history
- Large volume aspiration
- Depressed level of consciousness
- Supine position

3.4.2. Empirical Antibiotic Treatment:

1. Patients without risk factors with mild or moderate pneumonia starting at any time or with early-onset severe pneumonia, Community Acquired Pneumonia
   - Cefuroxime

2. Patients with specific risk factors with mild or moderate pneumonia starting at any time
   - Cefipime plus Amikacin

3. Patients with early-onset severe pneumonia and specific risk factors or late-onset severe pneumonia
   - Cefipime plus Amikacin

4. Aspiration Pneumonia
   - Cefipime

Table 6: Specific antibiotic treatment after culture is available

Micro-organism	First-line Antimicrobial	Alternative Antimicrobials	Treatment for Resistant Strains
Streptococcus pneumoniae	Semisynthetic penicillins (e.g. penicillin G or V)	First-generation cephalosporins (e.g. cefazolin), Macrolides (e.g. erythromycin, clindamycin)	Not specified; treatment based on susceptibility testing
Staphylococcus aureus	Penicilinase-resistant penicillins (e.g., Cloxacillin)	First- or second-generation cephalosporin (cefazolin, Cefuroxime) Macrolides (Clindamycin)	Methicillin-resistant Staphylococcus aureus (MRSA): Vancomycin
Pseudomonas	Aminoglycoside (e.g.,	Carbapenems (e.g.,	Not specified;

Micro-organism	First-line Antimicrobial	Alternative Antimicrobials	Treatment for Resistant Strains
aeruginosa	Tobramycin, gentamycin or amikacin) plus Extended spectrum penicillin (pipercillin)	Imipenem, meropenem) plus Aminoglycoside	treatment based on susceptibility testing
Hemophilus influenza	Second generation cephalosporin (e.g. Cefuroxime)	Fluoroquinolones (e.g. Ciprofloxacin), Macrolides (e.g. Erythromycin) Carbapenems (e.g. Meropenem)	Not specified; treatment based on susceptibility testing
Klebsiella pneumoniae	Extended spectrum penicillin Plus Aminoglycoside	Carbapenems Aminoglycoside Extended spectrum penicillin Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Not specified; treatment based on susceptibility testing
Escherichia coli	Fourth-generation cephalosporin (e.g., Cefepime) in severe illness: add Aminoglycoside	Penicillin (e.g., Ampcillin) with or without Aminoglycoside, Extended spectrum penicillin (e.g., Pipercillin)	Not specified; treatment based on susceptibility testing
Stenotrophomonas maltophilia	Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Tetracycline (e.g., *Minocycline), Fluoroquinolone (e.g. Ciprofloxacin)	Not specified; treatment based on susceptibility testing
Mycoplasma pneumoniae	Macrolides (e.g. erythromycin)	Macrolides (e.g. Clarithromycin, Azithromycin), Fluoroquinolone (e.g., *Levofloxacin)	Not specified; treatment based on susceptibility testing
Chlamydia pneumoniae	Tetracycline (e.g., Doxycycline)	Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole), Macrolides (e.g. Erythromycin), Fluoroquinolone (e.g. Ciprofloxacin)	Not specified; treatment based on susceptibility testing
Legionella pneumophilia	Macrolides (e.g. Erythromycin, Azithromycin), Fluoroquinolone (e.g., *Levofloxacin), Rifampin	Tetracycline (e.g. Doxycycline, Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Not specified; treatment based on susceptibility testing
Acinetobacter	Most of the cases are not pathogens and do not need treatment		Not specified

CHAPTER 4
GUIDELINES FOR THE NURSING STAFF AND PHYSIOTHERAPISTS

4.1. Introduction

The Neurosurgical Intensive Care unit has been selected as the site for this research due to the homogeneity of subjects admitted to your unit. The comatose patient has been identified as one of the high-risk groups for the development of ventilator-associated pneumonia. Your co-operation in this study is therefore essential for its success and your contribution is highly appreciated.

The day and night staff will undergo a training session on the aspects which involve you. If any questions or problems are experienced, you are welcome to contact the researcher. (Tel: Office number: 53572 or Cell number: 082 954 6122).

New staff members and Critical Care students may be allocated to the Neurosurgical Intensive Care Unit. The researcher will train these rotating staff as they are allocated to the unit.

4.2. Nursing care and physiotherapy

The Neurosurgical Intensive Care Unit will be supplied with the stock listed in Table 7 below, before the subject is admitted. The nursing staff is responsible to connect the ventilator circuit, the filters and the closed multi-use catheter system.

Table 7: Stock list

1. Disposable ventilator circuit
2. Closed multi-use catheter system
3. Bacterial filter for inspiratory leg of the ventilator circuit
4. Fischer and Packel humidifier
5. Fischer and Packel humidifier cable
6. Temperature cable for monitor system
7. Disposable temperature probe
8. Yankuare suction tip
9. Endotracheal aspirate collection tube
10. Cuff pressure monitor
11. Standard operating procedure manual
12. Daily Procedure form

4.2.1. Admission of the subject from theatre or after intubation

In this section the preparation of the ventilator and admission of the subject will be discussed.

4.2.1.1. Preparation of the ventilator

The nursing staff is responsible for the preparation of the ventilator.

Type of ventilator

The Puritan Bennett 7200 and the Newport Wave model E200 will be utilised in the study. The nursing staff will determine the ventilator used according to availability of ventilators.

Ventilator circuits and bacterial filters
Disposable ventilator circuits will be used. The researcher will provide the ventilator circuit and a bacterial filter for the inspiratory leg of the ventilator circuit before the admission of the subject to the Neurosurgical Intensive Care Unit. The bacterial filters routinely used, should be connected to the expiratory leg in the case of the puritan Bennet 7200 ventilator.

The circuit should be changed every 7th day or when the circuit is visibly soiled. The date for the change of the ventilator circuit will be indicated on a little card, attached to the ventilator circuit. The physiotherapist is responsible to change the disposable circuits and record it on the *Daily Procedure form* (Addendum 5). Both the inspiratory and expiratory filters should also be changed every 7 days.

Humidification
The Respiratory Humidifier Fisher and Pagal MR 700 humidification system must be used and all temperatures set at 39 ^{0} C. A 1liter bag of sterile water for irrigation must be connected to the humidification system and replaced when empty. This ensures that pulmonary secretions are humidified to prevent blocking of the endotracheal tube.

Ventilator settings
The mode of ventilation is synchronised intermittent mandatory ventilation and the type of ventilation will be volume-controlled ventilation. (Other ventilation modes can also be used if indicated.)

- Tidal volume is generally calculated in millilitres according to the formula of 6 to 8ml x ideal body weight in kilograms.
- The frequencies are usually initiated at ten rates per minute. The rate will be weaned down by two rates per minute until 4 rates. These changes should be made according to blood gas results or patient condition. The ventilator subject should be switched to spontaneous breathing after successfully weaning the subject.
- The FiO_2 is usually set at 0,40, but must be changed according to the blood gas results or patient condition.
- A pressure support of 8 cm H_2O is usually applied. This setting may be changed according to the patient's particular needs.
- Peak-flow setting may vary between 40 to 60 L/min.
- Changes will be made according the blood gas results, the physician's prescription and/or patient's condition.

4.2.1.2. Admission of the subject from theatre

On admission the patient should be connected to the ventilator and monitor. Routine nursing admission care should be provided, the patient should be stabilized and immediate orders carried out, before the following is performed.

Blood sampling of full blood count from arterial line

Blood sampling of the full blood count should take place according to the following procedure:

a) Preparation

1. Open two sterile 5 ml syringes in a sterile kidney receiver, a 5 ml full blood count collecting tube (purple tube), and sterile cotton swabs.
2. Wash your hands.
3. Put on gloves.

b) Procedure

1. Disconnect the cap from the three-way stopcock nearest to the arterial cannula.
2. Clean open end of the three-way stopcock with Hibitane® and sterile swab.
3. Connect 5 ml syringe to the three-way stopcock. Turn three-way stopcock in the direction of the artery.
4. Aspirate heparin solution from arterial line until undiluted blood is aspirate. Aspirated another 1 ml of blood. Sample 5ml of blood with second syringe and inject blood into purple collecting tube. Other samples may be taken at this time. Flush arterial line with heparinized 0.9% Sodium chloride solution (in pressure system).
5. Identify the purple collecting tube with the patient details.
6. Discard the used syringes and swaps.
7. Request laboratory order form under Haematology on the Meditech (Information Technology) system.
8. Put the blood sample together with order form in a plastic bag and send it off to the emergency Haematology laboratory.
9. Record the sampling of the fullblood count on the Daily Procedure form.

Chest X-ray

1. After admission of the patient, request a mobile chest X-ray.
2. When the chest X-ray is received from the X-ray department, ensure correct positioning of the endotracheal tube. Ensure that the tip of the endotracheal tube is 2.5 to 5cm above the carina.
3. In case of wrong positioning of endotracheal tube, contact the Neurosurgeon to correct the positioning of the endotracheal tube. Subglottic suctioning should be performed before the cuff is deflated for repositioning of the tube.

Connection of the closed multi-use catheter system

The closed multi-use catheter system is connected to the endotracheal tube before the endotracheal aspirate has been collected.

a) Procedure

1. Wash hands.
2. Open wrapping of the closed multi-use catheter system without touching the catheter.
3. Take the closed multi-use catheter system from wrapping by handling it on the sheath area.
4. Connect the closed multi-use catheter system to the endotracheal tube and the ventilator circuit.

Sampling of the endotracheal aspirate

An endotracheal aspirate should be collected post-operative. For the collection of endotracheal aspirate the closed multi-use catheter suction procedure should be utilised.

a) Preparation

1. Perform subglottic suctioning before the endotracheal suctioning procedure (See 4.2.2.4 for procedure).
2. Pre-oxygenate the subject by setting the oxygen on 100% and set rate at 10/minute.
3. Connect the endotracheal aspirate collector (Luki tube) to the closed-system suction catheter and suction tubing of suction bottle. Switch on the suction bottle and ensure a negative pressure of 80-to100 mgHg.
4. Prepare the sterile water for rinsing of suction catheter.

(Maintain sterility throughout preparation by not touching the connection ends of equipment)

b) Procedure

1. Wash your hands.
2. Introduce suction tube into endotracheal tube until the carina is reached. Pull the suction catheter 1 cm back with a turning movement and apply vacuum. Stabilise the endotracheal tube with the non-dominant hand.
3. Hold the endotracheal aspirate collection tube vertical. Apply suctioning by depressing the control valve.
4. When sample is obtained, allow assistant to disconnect the collection tube from the suction catheter in an aseptic manner. The assistant connects the tube of the aspirate tube to the open end. The assistant identifies the sample with subject's registration number.
5. Connect the closed multi-use catheter system to the suction tubing of the suction apparatus. Perform the suctioning procedure. (See 4.2.2.5).
6. Do not suction longer than 15 sec.
7. Evaluate ECG continuously.
8. Withdraw suction catheter totally from the endotracheal tube. Rinse the suction catheter through by injecting sterile water into the Y-port while applying suctioning.
9. Disconnect the catheter from the suction tube.
10. Cap the proximal end of the closed multi-use catheter system.
11. Put suction tube back in Hibitane ® solution.
12. Ensure that oxygen and rates are set to the previous setting. Check ventilator pressures.
13. Record the sampling on the Daily Procedure form with a ✓.
14. Request the necessary forms on the Meditech system.
15. Send the sample as soon as possible to the Emergency Laboratory on the fourth floor.

Insertion of the rectal temperature probe

The disposable rectal temperature probe should be inserted at admission.

a) Preparation

1. Put on gloves
2. Open rectal temperature probe packaging
3. Lubricate the probe with KY Jelly ®
4. Turn the subject on his/her side

b) Procedure

1. Insert the rectal temperature probe 4-5cm into the rectum
2. Turn patient on his/her back
3. Connect the rectal temperature probe to the temperature cable
4. Connect the temperature cable to the monitor at the temperature probe site and ensure a temperature reading on the monitor
5. Record the patient temperature on the patient vital sign form and Daily Procedure form.

4.2.2. Daily nursing care of the subjects

The patient should receive the routine nursing care as described in the policies and procedures of the Intensive Care Department. These aspects will be highlighted due to their importance to the research.

4.2.2.1. Mouth care

Mouth care of the subject should be performed every 6 hours as poor mouth hygiene increases the risk of developing nosocomial pneumonia (Fourrier, *et al.* 1998:301).

a) Preparation

1. Connect the Yankuare suction tip to the suction tubing.
2. Switch suction apparatus on.

b) Procedure

1. Inject 10 ml of the Hibident® solution into the mouth while applying suctioning with the Yankuare suction tip
2. Record the performance of the procedure on the Daily Procedure form.

4.2.2.2. Position subject at 20^0 to 30^0 supine

The patient should be positioned supine at 20^0 or 30^0 according to the prescription of the Neurosurgeon. Use the provided template (Figure 5) to ensure the correct positioning. Select the template according to the prescription of the Neurosurgeon. Match the template to the frame of the horizontal portion of the bed. Turn the head-end of the bed until the correct level is reached. If any changes were made to the bed level, the position of the subject should be aligned again.

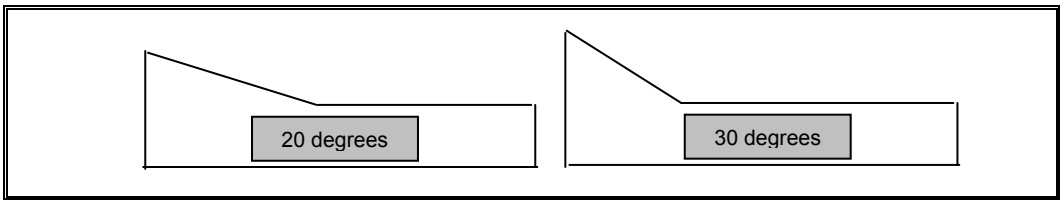

Figure 5: Example of templates for positioning of head portion of bed

4.2.2.3. Securing of the endotracheal tube

The purpose of securing the endotracheal tube is two-fold: firstly, to prevent extubation and secondly to prevent up and down movement of the endotracheal tube. Movement of the endotracheal tube causes leaking of subglottic secretions past the endotracheal tube cuff.

Preventative measures should be taken to prevent extubation or self-extubation of the subject at all times, as re-intubation is one of the causes of ventilator-associated pneumonia. Re-intubation is a withdrawal criterion of the research

The plaster that stabilizes the endotracheal tube should be cut according to Figure 6 and securely applied around the head and the endotracheal tube. Endotracheal tube plaster should be changed daily, when soiled and when it is not securing the endotracheal tube sufficiently.

a) Preparation of plaster

1. Cut the plaster ± 60cm long and ± 3cm wide.
2. Cut a piece of plaster about 20cm long and ± 3cm long. Apply this piece in the middle of the previously mentioned plaster.
3. Cut both ends of the long plaster in half down the centre for about 20cm.

b) Application of plaster

1. Apply the plaster as follows to the subject. The middle of the plaster is positioned behind the head of the subject.
2. Apply one half of the left leg of the plaster directly to the skin of the subject over the upper lip area.
3. Apply the half of the right leg directly onto the skin of the subject and around the endotracheal tube.
4. Apply the other half of the left leg directly onto the skin and around the endotracheal tube.
5. Lastly, apply the other half of right leg directly onto the skin of the subject and over the upper lip area.

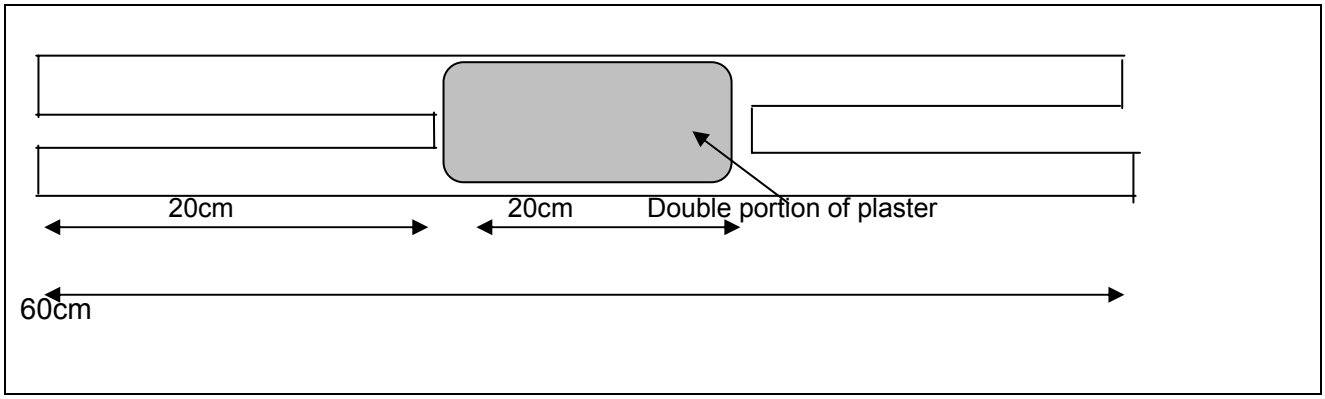

Figure 6: Outline of plaster for stabilization of the endotracheal tube.

4.2.2.4. Subglottic suctioning

Subglottic suctioning must be performed every two hours or when deemed necessary, more frequently.

a) Preparation

1. Connect the subglottic suctioning connection to the suction tubing of a Gabler suction device.
2. Open the Gabler suction device.

b) Procedure

1. Apply suctioning at a pressure of 100mg Hg for 8seconds. Repeat process every 20sec until no further secretions are aspirated.

2. If blockage of the Evac lumen is suspected, it may be cleared by injecting 1 ml of **air** through the lumen to maintain patency.
3. Record the procedure on the Daily Procedure form.

4.2.2.5. Routine endotracheal suctioning

The closed-system suction device must be utilised for routine suctioning of the patient. Endotracheal suctioning is performed at the discretion of the nursing staff and the physiotherapist. The condition of the patient and amount of secretions will determine the frequency of the suctioning procedure.

The figure below is a photograph of the closed multi-use catheter system used in the study.

Fig.7: Closed multi-use catheter system (Mallinckrodt Dar, 2002:4)

See the procedure of connecting the closed multi-use catheter system in 4.2.1.2. The closed multi-use catheter system must be changed ever morning or when blocked by the physiotherapist.

a) Preparation

Wash your hands.

Prepare solution for bronchial lavage and 5ml syringe with sterile water for rinsing of the suction catheter. Maintain sterility of the tips of the syringes throughout the procedure.

Set the ventilator on 100% oxygen and rates on 10/minute for the duration of the procedure.

Perform the subglottic suctioning procedure (See 4.2.2.4.)

b) Procedure

1. Connect the closed multi-use catheter system to the suctioning tubing of the Gabler suction device. Open the Gabler suction device to a negative pressure of 80 to 100mg Hg.
2. Open lid of the control valve.
3. Stabilise the endotracheal tube with the non-dominant hand.
4. Advance the closed multi-use catheter system with the dominant hand into the endotracheal tube. Handle the suction catheter with the plastic sheath. When the carina is reached, withdraw the catheter 1cm and fully depress the control valve to apply negative pressure.
5. Withdraw the closed multi-use catheter system with a turning movement, while stabilizing the endotracheal tube and negative pressure is applied. Do not apply the

suctioning longer than 15sec. at a time. Withdraw the suction catheter totally from the endotracheal tube until the T-piece is reached.
6. Allow for mechanical ventilation to take place, either from the set values or by utilising the manual ventilation button.
7. For bronchial lavage, advance the catheter into the endotracheal tube. Connect syringe with solution for lavage to the Y-Piece. Instil 2 to 3ml of the solution into the endotracheal tube. Allow the ventilator to cycle. Continue to advance the suction catheter into the endotracheal tube and perform suctioning as already described.
8. Perform the procedure as many times as needed by the particular subject.
9. Evaluate the ECG continuously.
10. After the suctioning procedure is completed, the suction catheter should be flushed with sterile water. Withdraw the suction catheter from the endotracheal tube. Depress the control valve. **Slowly** inject 5 ml of sterile water into the catheter while depressing the control valve.
11. Close the lid of the control valve and disconnect the suction tubing of the Gabler suction device. Put the suction tubing into the container of Hibitane® solution.
12. Cap the suction catheter.
13. Remove the 5ml syringe from the Y-piece and re-cap the port.
14. Reset the oxygen delivery and the rates on the ventilator to the previous value.
15. Wash your hands.

After the suctioning procedure has been performed, the procedure and the appearance of secretions are recorded on the Daily Procedure form of the subject.

4.2.2.6. Collection of an endotracheal aspirate on Mondays and Thursdays

The endotracheal aspirate sample is obtained on Mondays and Thursdays just after the new closed multi-use catheter system has been changed. It is the responsibility of the physiotherapist to perform this procedure.

a) Preparation

1. Perform the closed multi-use catheter system suctioning procedure as explained under 4.2.2.5.
2. Connect the new closed multi-use catheter system. (See 4.2.1.2)

(Maintain sterility throughout preparation by the non-touch method)

b) Procedure

1. For sampling of the endotracheal aspirate see 4.2.1.2.

4.2.2.7. Two-hourly cuff pressure monitoring

Cuff pressure is the pressure in the endotracheal tube cuff after inflation with air. The cuff pressure of the patients intubated with the Hi- Contour ^{TM} (Mallinckrodt, Athlone, Ireland) endotracheal tube and the HiLo Evac^{TM} (Mallinckrodt, Athlone, Ireland) endotracheal tube must be measured and maintained between 25 and 33 cmH_2O (Boggs & Woodridge-King, 1993:44). Cuff pressure measurement of the HiLo Evac^{TM} (Mallinckrodt, Athlone, Ireland) endotracheal tube with Lanz valve is not necessary as the valve maintains the pressure in the cuff automatically. (The researcher will remind you when the patient has been intubated with this type of endotracheal tube)

Use the provided cuff pressure manometers for the measuring of cuff pressures (HiLo cuff pressure gauge).

a) Procedure

1. Connect the cuff manometer line to the inflation valve of the endotracheal tube.
2. Measure the cuff pressure.
3. If cuff pressure is less than 25cmH_2O inflate the cuff with the manometer until the correct cuff pressure is reached.
4. If the pressure is higher than 33cmH_2O, open the release valve on the left side of the manometer until correct pressure is reached. Leave the manometer connected as air escapes when the manometer is connected and disconnected. Be careful not to over-deflate the cuff.

Perform this procedure every 2 hours and record cuff pressure on Daily Procedure form.

4.2.2.8. Daily Chest X-ray

Daily mobile chest X-rays should be obtained daily, preferably early in the morning. Daily chest X-rays should be evaluated for the positioning of the endotracheal tube and for complications of mechanical ventilation, like a pneumothorax etc. Management will be the same as the chest X-ray under 4.2.1.2.

The blind investigator will evaluate the chest X-rays, the temperature, the appearance of the secretions and laboratory results for the presence of ventilator-associated pneumonia.

4.2.2.9. Taking of full blood counts on Mondays and Thursdays

A full blood count should be taken every Monday or Thursday from the subject's arterial line.

For preparation and procedure see 4.2.1.2.

4.2.3. Summery

It is important that you should adhere to the following at all times:

- Wash hands before and after touching the subject
- Adhere to aseptic techniques at all times

Your involvement and effort in this research is very important. Without your dedication and assistance this research will not be possible. If a problem arises, please consult the Standard Operating Procedure Manual. If you cannot solve the problem yourself, you are welcome to phone me on the telephone numbers provided.

CHAPTER 5
GUIDELINES FOR THE RESEARCHER

It is the responsibility of the researcher to ensure that all the contributors adhere to the research design. Furthermore, the researcher should collect the baseline information, laboratory results and the records of the Daily Procedure form. This information is then provided to the blind investigator. The researcher will then analyse data and write and report on the findings of the research.

5.1. IDENTIFICATION OF SUBJECT

After the Neurosurgeon has reported a prospective candidate to the researcher, the researcher will visit the subject. The researcher will then explain to the patient the purpose of the procedure, and other adverse effects related to the research. The researcher (or translator) will then read the contents of the consent form to the subject. When consent has been obtained, the subject will sign the consent form in the presence of a witness.

When the subject is not able to give consent, the researcher will obtain written or telephonic consent from the spouse, parent, or adult children. A copy of the consent form will be given to the patient or the family member. A notice that the subject is participating in this particular research will be put into the file of the subject.

Telephonic consent can also be obtained in the case if the subject's direct family is not present. The telephonic consent must be repeated to a witness.

5.2. Screening

The subject will be screened for the presence of immune suppression and for the presence of a presence of a pre-existing pneumonia

5.2.1. Sampling blood for the full blood count

a) Procedure

1. Wash your hands
2. Put on protective gloves
3. Prepare the skin with an alcohol swap
4. The blood sample will be obtained from the subject via venous puncture in a 5ml heparinzed purple collection tube.
5. Apply a swab to the punctured area and secure with plaster
6. The subject's name and hospital number identify the blood sample.
7. A request form must be completed for a fullblood count.
8. Put the samples and request forms into a plastic bag.
9. The sample must be sent to the Haematology Laboratory as soon as possible.
10. The laboratory results will be obtained from the Meditech Information Technology system.
11. The results of the leucocytes, neutrophyls, and lymphocytes will be recorded on the baseline assessment form.

5.2.2. Taking of a chest X-ray

The researcher will ensure that a chest X-ray is taken before surgery. As this is a routine procedure, the researcher will ensure that there is no duplication.

5.2.3. Baseline information and final result form

The researcher completes the *Baseline Information* (Addendum 4) and results by the information provided by the subject or the family member of the subject by the subject's file and nursing records. The researcher will ask the subject the questions listed in the *Baseline information* form. If the subject cannot answer these questions, the family and the neurosurgeon will be consulted regarding the answers.

The researcher completes the *Barthel Index* questionnaire (Addendum 7) after Addendum 4 has been completed. The researcher must not lead the subject in the answers.

5.2.3.1. Medication suppressing the immune system

The researcher will ask the subject about medication taken. The researcher will also check the admission notes and prescription chart of the subject. The researcher will check for the prescription of antibiotics, steroid therapy and H_2 antagonists.

5.2.3.2. Evaluation of suppression of level of consciousness

The researcher will ask questions as follows:

1. What is the time, morning, afternoon or night, what season is it?
2. In which town are you presently?
3. What is your wife's/ husband's or parent's name? What is your name? (Information given will be confirmed with a family member.)

5.2.3.3. Anthropometrical assessment

Anthropometric measurements should be taken in the sitting position or if the subject is unable to sit, the subject should be positioned on his left side and right side should be measured.

Subcutaneous fat (Skinfold thickness)

a) General guidelines for measuring skinfold thickness

1. Measure skinfold thickness on the right side of the patient. (Use the left side if right side paralysis is present.)
2. Mark the site for measurement, when identified.
3. Grasp the skinfold firmly between the thumb and the index finger of the left hand 1 cm from the site to be measured. This pressure should be maintained during the measurement
4. The calliper should be held in the right hand with the dial clearly visible and the measurement should be about 1 cm from the fingers.
5. The calliper should not be positioned too deep or too shallow, but at the point of a double skinfold.
6. When taking the reading, avoid making a parallax error.
7. Take at least two measurements per site 15 seconds apart. Value acquired should not be more than 1 mm apart. If a difference is experienced, keep on measuring until a consistency is reached (Lee & Nieman, 1993:138-139).

b) Triceps skinfold thickness (TSF)

The triceps skinfold measurement is taken midway between the tip of the and the shoulder. The arm should be held vertically with the skinfold parallel to the arm. The hand should be facing anterior. Measure the arm from the acronomion process of the scapula to the olecranon process of the ulna (Lee & Nieman, 1993:138-139).

Divide this distance in two and mark the distance from the acronomion on the mid-arm. Measure with a skinfold calliper the thickness of posterior aspect of the arm 4 seconds after application of calliper (Mahan & Escott-Stump, 1996:372).

c) Subscapular skinfold thickness

Position the arm of the patient at his back. Identify the position of the scapula. The site for measurement is 1 cm below this point. The calliper should be applied 45 ^{0} angle to the long axis and to the right (Lee & Nieman, 1993:140). The patient ideally should sit, but if not possible, the patient must turn on his left side and be measured on the right side.

Add the triceps and subscapular skinfold measurements and compare to the percentiles of the related gender (see Addendum 8).

Circumference measurements

a) Mid-upper arm circumference

Measure the arm from the acronomion process of the scapula to the tip of the elbow. Divide this distance in two and mark the distance from the acronomion on the mid-arm. Measure the mid-arm circumference at this level.

Connect the mid-upper arm measurement and the triceps skinfold measurement and obtain the arm muscle area (measured in cm^2) on the scale (Addendum 8). Compare the arm muscle area with the respective gender percentile (Addendum 8) (Frisancho, 1999: 22,87,90,103, 106).

5.3. Assignment to study group

After all the information has been completed the subject will be screened according to the inclusion and exclusion criteria. The subject who meets the inclusion criteria will be assigned to the study group according to the research design.

5.4. Provide stock to theatre staff and intensive care unit

The following stock should be made available to the anaesthesia nurse:

- Selected type of endotracheal tube in a size 7.5, 8.0 and 8.5
- Bacterial filter
- Cuff pressure monitor
- Anaesthesia form
- Standard Operating Procedure Manual

The following stock should be made available to the nursing staff of the Intensive Care Unit:

- Disposable ventilator circuit
- Closed multi-use catheter system
- Bacterial filter
- Fischer and Packel humidifier
- Fischer and Packel cable
- Disposable rectal probe
- Temperature cable
- Yankuare
- Endotracheal aspirate collection tube
- Daily Procedure form
- Standard Operating Procedure Manual

5.5. Collection of data

5.5.1. Procedures performed

The researcher collects the data as completed by the nursing staff and the physiotherapists on the *Daily Procedure* form. The appearance of pulmonary secretions, as recorded by the nursing staff and the physiotherapist will be recorded on the above-mentioned form.

5.5.2. Laboratory data

The researcher obtains the laboratory results from Meditech programme on the Hospital Information System (Information Technology). A printout of these results will be filed with the subject's documentation for further moderation. The researcher must record the laboratory results on the *Information for Blind Investigator Regarding the Diagnosis of Ventilator-Associated Pneumonia*. The blind investigator records his findings on the *Information for Blind Investigator Regarding the Diagnosis of Ventilator-Associated Pneumonia.*

5.5.3. Chest X-rays

The researcher meets weekly with the blind investigator. The researcher will then provide the chest X-rays and the completed Information for *Blind Investigator Regarding the Diagnosis of Ventilator-Associated Pneumonia form* of the subject.

5.5.4. Management of research records

All documentation should be considered as confidential and store should be in a safe place. The researcher will submit all documentation related to the study for moderation and auditing by the sponsor.

The researcher is also responsible to keep record of the stock provided by the sponsor and the application thereof.

After completion of the research the documents must be kept in a safe and secure place for five years.

CHAPTER 6
GUIDELINES FOR THE BLIND INVESTIGATOR

The blind investigator is responsible for drawing up the guidelines for the prescription of antibiotics. The Neurosurgeon may contact the blind investigator if deemed necessary. The blind investigator is then responsible for the Neurosurgeon on the prescription of the antibiotics. The blind investigator may not see the subject, but may contact the Neurosurgeon if more information about the clinical picture of the subject is necessary.

The sponsor will appoint the blind investigator. The blind investigator is responsible for make the diagnosis of a ventilator-associated pneumonia. The researcher will provide the blind investigator with the information necessary to making the diagnosis. The blind investigator may contact the neurosurgeon concerning the physical condition of the patient, if deemed necessary.

The blind investigator will meet with the researcher on a weekly basis and will examine the records as provided by the researcher (see 4.3.). The blind investigator will make the diagnosis of a ventilator-associated pneumonia for research purposes.

6.1 Diagnosis of ventilator-associated

A ventilator-associated pneumonia will be diagnosed if the listed criteria apply.

1) A new progressive infiltration is seen on chest X-ray
   and

2) A positive endotracheal aspirate culture of a pathogen, associated with:
3) Purulent endotracheal secretions observed during suctioning
   and

4) Pyrexia (rectal temperature of $\geq 38{,}3^0$C) or hypothermia (rectal temperature of $< 36^0$C)
   or

   Leucocytosis of $>10x10^9$ /L

(Cook, Jonghe, Brochard, & Brun-Buisson, 1998:783; Young & Ridley, 1999:1184).

A second blind investigator will be appointed for circumstances where the first mentioned blind investigator is not available. This second blind investigator should adhere to the prescription of antibiotics, by the first blind investigator.

6.2. Guideline for the prescription of antimicrobial therapy.

The following section has been compiled by Dr J.G.H. Lups as guidelines for the diagnosis of ventilator associated pneumonia and the administration of antimicrobial drugs.

Guidelines for management of Ventilator-associated Pneumonia

Study:
The Effects of three types of Endotracheal tubes on Ventilator-associated Pneumonia

Objective:
To establish guidelines for the prescription of antibiotics for subjects of the study, in case of a ventilator-associated pneumonia

Definitions:

1. **Ventilator-associated Pneumonia (VAP)**
    - As defined in the study protocol

2. **Early Onset ventilator-associated pneumonia**
    - If present in a patient on mechanical ventilation within 48 to 72 hours after intubation

3. **Late Onset ventilator-associated pneumonia**
    - Ventilator-associated pneumonia that develops 72 hours after intubation

4. **Severe Pneumonia**
    - Respiratory rate > 30 breaths/min
    - Low blood pressure
      Systolic < 90 mmHg
      Diastolic < 60 mmHg
      Need for vasopressors > 4 hours
    - Multilobar consolidation
    - Extrahoracic septic complications
    - Confusion or decreased consciousness

5. **Patients at risk of developing VAP**
    - Older than 60 years of age
    - Chronic lung disease or systemic disease
    - Recent antibiotic history
    - Large volume aspiration
    - Depressed level of consciousness
    - Supine position

Empirical Antibiotic Treatment:

6. Patients without risk factors with mild or moderate pneumonia starting at any time or with early-onset severe pneumonia, Community Acquired Pneumonia
    - Cefuroxime

7. Patients with specific risk factors with mild or moderate pneumonia starting at any time
    - Cefipime plus Amikacin

8. Patients with early-onset severe pneumonia and specific risk factors or late-onset severe pneumonia
    - Cefipime plus Amikacin

9. Aspiration Pneumonia
    - Cefipime

Table 8: Specific antibiotic treatment after culture is available:

Micro-organism	First-line Antimicrobial	Alternative Antimicrobials	Treatment for Resistant Strains
Streptococcus pneumoniae	Semisynthetic penicillins (e.g. penicillin G or V)	First-generation cephalosporins (e.g. cefazolin), Macrolides (e.g. erythromycin, clindamycin)	Not specified; treatment based on susceptibility testing
Staphylococcus aureus	Penicilinase-resistant penicillins (e.g., Cloxacillin)	First- or second-generation cephalosporin (cefazolin, Cefuroxime) Macrolides (Clindamycin)	Methicillin-resistant Staphylococcus aureus (MRSA): Vancomycin
Pseudomonas aeruginosa	Aminoglycoside (e.g., Tobramycin, gentamycin or amikacin) plus Extended spectrum penicillin (pipercillin)	Carbapenems (e.g., Imipenem, meropenem) plus Aminoglycoside	Not specified; treatment based on susceptibility testing
Hemophilus influenza	Second generation cephalosporin (e.g. Cefuroxime)	Fluoroquinolones (e.g. Ciprofloxacin), Macrolides (e.g. Erythromycin) Carbapenems (e.g. Meropenem)	Not specified; treatment based on susceptibility testing
Klebsiella pneumoniae	Extended spectrum penicillin Plus Aminoglycoside	Carbapenems Aminoglycoside Extended spectrum penicillin Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Not specified; treatment based on susceptibility testing
Escherichia coli	Fourth-generation cephalosporin (e.g., Cefepime) in severe illness: add Aminoglycoside	Penicillin (e.g., Ampcillin) with or without Aminoglycoside, Extended spectrum penicillin (e.g., Pipercillin)	Not specified; treatment based on susceptibility testing
Stenotrophomonas maltophilia	Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Tetracycline (e.g., *Minocycline), Fluoroquinolone (e.g.	Not specified; treatment based on susceptibility testing

		Ciprofloxacin)	
Mycoplasma pneumoniae	Macrolides (e.g. erythromycin)	Macrolides (e.g. Clarithromycin, Azithromycin), Fluoroquinolone (e.g., *Levofloxacin)	Not specified; treatment based on susceptibility testing
Chlamydia pneumoniae	Tetracycline (e.g., Doxycycline)	Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole), Macrolides (e.g. Erythromycin), Fluoroquinolone (e.g. Ciprofloxacin)	Not specified; treatment based on susceptibility testing
Legionella pneumophilia	Macrolides (e.g. Erythromycin, Azithromycin), Fluoroquinolone (e.g., *Levofloxacin), Rifampin	Tetracycline (e.g. Doxycycline, Sulfonamide (e.g., Trimethaprim-Sulfamethoxazole)	Not specified; treatment based on susceptibility testing
Acinetobacter	Most of the cases are not pathogens and do not need treatment		Not specified

CHAPTER 7
GUIDELINES FOR THE MONITOR

The sponsor appoints the monitor, whose responsibility it is to communicate with the researcher and the sponsor. The monitor should meet with the researcher every two weeks.

7.1. Responsibilities of the monitor

- The monitor has to oversee that there is adherence to the standard operating procedures.
- The monitor must keep record of visits, telephone calls and letters to the researcher.
- The monitor or other contact persons should be available to the research at all times.
- Before the trial is commenced, the monitor has to visit the site to ensure that the site is suitable for the research.
- The monitor should check the storage of the equipment.
- The monitor should check recording of data for correctness and completeness.
- The monitor should check that the staff is fully informed about the procedures of the research design.
- The monitor should ensure that the researcher has all the stock necessary for the research.

7.2 During the research

The monitor should:

- Visit the researcher at least monthly,
- Meet the staff involved with the data collection,
- Check if informed consent was obtained,
- Ensure that all equipment was applied as according to the research design,
- Ensure that the researcher retains study documentation,
- Ensure correct documentation of source data like; labelling, dating, signatures,
- Ensure that all documentation is managed in a confidential manner,
- Ensure that all problems which arise are discussed and
- Document progress of the study, adverse events and withdrawal from the study.

7.3 After the research

The monitor should ensure that:

- Documents are kept safely where confidentiality can be ensured
- Unused equipment is returned to the sponsor and
- Reports are given to the relevant parties

CHAPTER 8
GUIDELINE FOR THE AUDITOR

8.1. RESPONSIBILITIES

The purpose of the auditor is to evaluate trial conduct and compliance with the research design, standard operating procedures and with guidelines of Good Clinical Practices. The auditor should visit the site every three months and compile a report on the progress of the research to the sponsor. If non-compliance to the research exists the auditor should report it to the ethics committee and the sponsor.

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ADDENDUM 2

RECORD OF SUBJECTS AND INVENTORY LIST

1. **RECORD OF SUBJECTS SCREENED**
2. **RECORD OF SUBJECTS ENROLLED**
3. **INVENTORY LIST**

1. RECORD OF SUBJECTS SCREENED

NUMBER	SUBJECT INITIALS	DATE OF SCREENING	STUDY NUMBER	STUDY GROUP	COMMENT
1	MZ	09/04/03	-	-	Not operated
2	PH	10/04/03	-	-	Withdrawal-extubated post-op
3	TG	15/04/03	-	-	ICU full
4	ML	30/04/03	Pilot I	I	
5	NSE	05/05/03	Pilot II	I	
6	SMS	30/05/03	Pilot III	I	
7	HM	02/06/03			Not operated
8	MSZ	09/06/03	2	I	
9	NLM	09/06/03	1	I	
10	TG	11/06/03	3	I	Screened previously
11	PG	18/06/03	4	I	
12	KMS	23/06/03			Not operated-coil
13	TR	23/06/03	6	I	
14	SM	02/07/03			Withdrawal-Extubated post-op
15	MZ	07/07/03			Extubated post -op
16	PC	08/07/03	5	I	Intubated in ICU
17	ME	09/07/03	7	I	
18	CC	18/07/03	45	III	Intubated with Hi-contour ET
19	SI	19/07/03			Withdrawal – Lymphocytopenia
20	KMS	29/07/03	8	I	
21	PKM	29/07/03	9	I	
22	BAE	11/08/03			Withdrawal-Extubated post-op
23	Kj	12/08/03			Withdrawal-Extubated post-op
24	SD	14/08/03			Withdrawal-Extubated after 6 hours
25	RML	25/08/03			Not operated
26	SEJ	26/08/03	10	I	
27	PG	08/09/03	11	I	
28	VVL	01/09/03	46	III	Intubated with tube of Hi-Contour ET
29	MI	16/09/03			Refused operation
30	MP	29/09/03			Withdrawal-Extubated post-op
31	RDR	20/10/03	12	I	
32	TNS	16/10/03			Not operated
33	BE	04/11/03			Withdrawal-Extubated post-op
34	MJL	16/10/03	13	I	
35	RA	24/11/03			Not operated AVM
36	TMA	05/11/03	14	I	
37	SJ	26/11/03	15	I	
38	TJ	26/11/03	47	III	
39	MMJ	11/12/03	48	III	
40	SJD	18/12/03			Withdrawal-Extubated post-op

NUMBER	SUBJECT INITIALS	DATE OF SCREENING	STUDY NUMBER	STUDY GROUP	COMMENT
41	MM	07/01/04			Withdrawal –extubated 2hours post-op
42	BC	18/02/04			Withdrawal-Extubated post-op
43	FKM	18/02/04			Withdrawal-Extubated post op
44	VJM	10/03/04			Withdrawal-Extubated post op
45	MSZ	28/01/04	49	III	
46	MI	13/12/04	51	III	
47	FJ	22/01/04	50	III	
48	MT	04/02/04	52	III	
49	KC	08/02/04	53	III	
50	DC	11/02/04	54	III	
51	MJM	11/03/04	55	III	
52	TRB	18/03/04			Withdrawal not operated
53	MDM	29/03/04	56	III	
54	KDP	29/03/04			Withdrawal Extubated post-op
55	RR	30/03/04	57	III	
56	DW	01/04/04	23	II	
57	PME	05/04/04	24	II	
58	KME	19/04/04			Withdrawal- Self-extubation
59	RMI	20/04/04	26	II	
60	MMM	28/04/04			Withdrawal-extubated post-op
61	LDL	10/05/04	25	II	
62	MPA	25/06/04	27	II	
63	RBL	02/06/04			Withdrawal-extubated post-op
64	PSI	03/06/04			Withdrawal-extubated post-op
65	PMS	09/06/04			Withdrawal-extubated post-op
66	SS	17/07/04			Withdrawal-extubated post-op
67	LSN	22/07/04	28	II	
68	MNR	22/07/04			Withdrawal-extubated post-op
69	WD	27/07/04			Withdrawal-extubated post-op
70	HCF	28/07/04			ICU full
71	DC	09/08/04			Withdrawal-extubated post-op

2. RECORD OF SUBJECTS ENROLLED

STUDY NR	STUDY GROUP	DATE SCREENED	DATE OPERATED	PLANNED 42 DAY FOLLOW UP	COMMENTS
P1	I	30/04/03	30/04/03	11/06/03	Pilot study
P2	I	05/05/03	06/05/03	17/06/03	Pilot study
P3	I	30/05/03	03/06/03	21/07/03	Pilot study
STUDY GROUP 1					
1	I	09/06/03	10/06/03	18/08/03	
2	I	09/06/03	11/06/03	28/07/03	
3	I	11/06/03	12/06/03	21/07/03	Died
4	I	18/06/03	19/06/03	28/07/03	
5	I	08/07/03	Not operated	-	Died
6	I	23/06/03	25/06/03	04/08/03	
7	I	09/07/03	10/07/03	19/08/03	
8	I	29/07/03	30/07/03	09/09/03	Died
9	I	29/07/03	01/08/03	10/09/03	
10	I	26/08/03	27/09/03	09/10/03	
11	I	08/09/03	09/09/03	22/10/03	
12	I	20/10//03	21/09/03	02/12/03	
13	I	16/10/03	21/10/03	02/12/03	
14	I	05/11/03	Not operated	-	Died
15	I	26/11/03	27/10/03	01/01/03	
STUDY GROUP 2					
23	2	01/04/04	02/04/04	14/05/04	
24	2	05/04/04	06/04/04	18/05/04	
25	2	10/05/04	11/05/04	-	Died before 42 days
26	2	20/04/04	04/05/04	15/06/04	
27	2	25/04/04	Not operated	20/06/04	
28	2	22/07/04	22/07/04	-	Died 23/07/04
STUDY GROUP 3					
45	3	18/07/03	14/07/03	29/08/04	
46	3	01/09/03	02/09/03		Died
47	3	26/11/03	02/12/03	13/01/04	
48	3	11/12/03	11/12/03	22/01/04	
49	3	28/01/04	29/01/04		Died
50	3	22/01/04	22/01/04	04/03/04	
51	3	13/12/04	22/01/04	08/03/04	
52	3	04/02/04	13/02/04	26/03/04	
53	3	08/02/04	08/02/04	23/03/04	
54	3	11/02/04	12/02/04	25/03/04	
55	3	11/03/04	11/03/04	22/04/04	
56	3	29/03/04	30/03/04		Died
57	3	29/03/04	Not operated	11/05/04	

3. INVENTORY

STOCK	SIZE	NUMBER RECEIVED	STOCK UTILIZED FOR RESEARCH	STOCK NOT USED	COMMENT
Endotracheal tubes					
HiLo Evac	7.5	10	7	3	Stock given back to sponsor
	8.0	20	17	3	Stock given back to sponsor
	8.5	10	2	8	Stock given back to sponsor
HiLo Lanz	7.5	10	7	3	Stock given back to sponsor
	8.0	10	8	2	Stock given back to sponsor
	8.5	10	1	9	Stock given back to sponsor
Hi-Contour	7.5	10	3	7	Stock given back to sponsor
	8.0	20	17	3	Stock given back to sponsor
	8.5	10	0	10	Stock given back to sponsor
Assorted stock					
Sterivent filiters		50	49	1	Stock given back to sponsor
Hygrobac filters		50	43	7	Stock given back to sponsor
Disposable ventilator circuit		50	44	6	Stock donated by sponsor to Neurosurgical Intensive care Unit
Closed multi-use system		80	80	0	Stock donated by sponsor to Neurosurgical Intensive care Unit
Disposable rectal thermometers		50	43	7	Stock donated by sponsor to Neurosurgical Intensive care Unit
Yankuaer suction tips		50	43	7	Stock donated by sponsor to Neurosurgical Intensive care Unit
Luki tubes		48	43	5	Stock donated by sponsor to Neurosurgical Intensive care Unit

ADDENDUM 3

ETHICAL CONSIDERATIONS

1. **DECLARATION OF HELSINKI**

2. **ENGLISH CONSENT FORM**

3. **AFRIKAANS CONSENT FORM**

4. **SOUTH-SOTHO CONSENT FORM**

5. **APPROVAL OF THE ETHICS COMMITTEE**

1. DECLARATION OF HELSINKI

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the52nd WMA General Assembly, Edinburgh, Scotland, October 2000
Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002

INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged

must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can

be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration

and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists. See footnote

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

FOOTNOTE:
NOTE OF CLARIFICATION ON PARAGRAPH 29 of the WMA DECLARATION OF HELSINKI

The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or

- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

Page back to paragraph 29.

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Somerset-West, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.

(ICH Guidelines, 2002:1)

2. ENGLISH CONSENT FORM

THE EFFECT OF THREE TYPES OF ENDOTRACHEAL TUBES ON VENTILATOR-ASSOCIATED PNEUMONIA

Researcher: M.J.J. Phillips

When a patient under goes a big operation, a pipe is put down the throat of the patient. This pipe (endotracheal tube) is connected to a breathing machine. This will help the patient to breathe. One of the problems is that patients who are put on a breathing machine can get a lung infection. This can lengthen the time a patient has to spend on a breathing machine as well as time that the patient has to stay in the intensive care unit and the hospital. It will also increase the hospital bills. In severe cases it may even lead to the death of a patient.

The reason of this research is to the see if there is a difference of lung infections in patients intubated with different types of tubes. Some of these tubes allow us to suction out the phlegm deep down in the throat. Tyco Healthcare sponsors the research. The company will assist with the research.

Sixty-six subjects (patients) that do not have a lung infection may be part of the research. The researcher will decide who may take part in the study. Those patients that take part in the study will be divided into three groups. The one group of patients will be intubated with the tube that is used in normal circumstances. The other two groups will receive a tube that helps us to remove the phlegm deep down in the throat of the patient. This procedure of the removal of phlegm, will be performed every two hours. The patient will not be aware of this. He/she will not experience any discomfort. The procedure will be performed until the tube is removed. If the subject gets a lung infection, the subject will be observed for other problems. This information will be compared. Except for suctioning out the phlegm, all the subjects will receive the same nursing care.

The researcher will ask you some questions before your surgery and write the answers down. After that the researcher will take some blood to see if your immune system works well. This may be painful or a blue area may develop where the blood was taken.

In this study, the researcher will write down the results of the blood and phlegm that were tested, the temperatures of the subject, pressures that was taken and the results of chest x-rays. A doctor will look at these results at say if the subject has a lung infection. The results of this research will assist the medical staff to improve care to patients and reduce medical costs.

The research method has been approved by the ethical committee of the Faculty of Health Sciences of the University of the Free State. The study does not pose any more dangers to the subject as the normal tube that is always used. Subjects in this research will be looked after very carefully while the research is done.

If you have any questions; you are welcome to ask me anything about the study or of being a subject. You may call Mrs. M.J.J Phillips at 082 954 6122 if you have any more questions.

Your name will not be put together with your results in the research. All information will be collected by the investigator, stored in a safe place and not shared with any other person without your permission.

You participation in this study is of your own free will: you are not forced to take part and you have the right to withdraw at any time without any unfair treatment. There will be no reward for taking part in this research. There are no fees to be paid to partake in this research.

I, …….. have read this consent form and of my own free will wants to take part in the study. I have been given a copy of this consent form.

……..	**…….**	**……..**
Subjects signature	**Place**	**Date**
…….		**……..**
Witness		**Date**
……..		**…….**
Researcher's signature		**Date**

Consent in proxy

I, ……. have read this consent form and give consent that my child/ husband/ wife/ father/mother …….. may participate in this study. I have been given a copy of this consent form.

……	**……**	**……**
Signature	**Place**	**Date**
……..		**…..……**
Witness		**Date**
……..		**……**
Researcher's signature		**Date**

Telephonic consent

The researcher has read the consent form to me. I, …… give consent that my child/ husband/ wife/ father/mother …….. may participate in this study. (A copy of the consent form will be put with the belongings of your relative.)

……..	**……**	**……..**
Signature of witness	**Place**	**Date**
……..		**…….**
Researcher's signature		**Date**

3. AFRIKAANS CONSENT FORM

DIE EFFEK VAN DRIE TIPES ENDOTRAGEALE BUISE OP VENTILATOR-GEASSOSIEERDE PNEUMONIE.

Navorser: M.J.J. Phillips

Wanneer ‘n pasiënt ‘n groot operasie ondergaan, word ‘n pyp in die lugweg van die pasiënt geplaas. Hierdie pyp (endotrageale buis) word aan ‘n asemhalings masjien gekoppel. Dit help die pasiënt om asem te haal. Een van die probleme wat ondervind word, is dat die pasiënt ‘n long infeksie kan ontwikkel. Dit kan veroorsaak dat die pasiënt ‘n langer periode op die asemhalings masjien en dus in die intensiewe sorg eenheid en hospitaal, spandeer. Dit sal dus ook ‘n styging in hospitaal onkostes tot gevolg hê. In erge gevalle mag die long infeksie lei tot die dood van die pasiënt.

Die rede vir hierdie navorsing is om te sien of daar ‘n verskil is in pasiënte geintubeer met verskillende tipes endotrageale buise. Sommige van hierdie endotrageale buise laat toe dat die slym diep agter in die keel uitgesuig kan word. Tyco Health Care ondersteun die navorsing. Die maatskappy sal ook met die navorsing help.

Ses-en-sestig proef persoon wat nie ‘n long-infeksie het nie, mag aan die navorsing deel neem. Die navorser besluit wie aan die navorsing mag deel neem. Die proef persoon wat aan die navorsing deel neem, word in drie groepe verdeel. Een groep proef persone sal met die buis wat gewoontlik gebruik word geintubeer word. Die twee ander groepe gaan met buise geintubeer word wat oor die vermoë beskik om slym diep uit die keel te verwyder. Die prosedure (verwydering van slym) sal elke twee ure geskied. Die proef persoon sal nie hiervan bewus wees nie. Hy/sy sal nie enige ongemak ervaar nie. Die prosedure sal uitgevoer word totdat die buis verwyder word. Indien die proef persoon ‘n infeksie ontwikkel sal proef persoon geobserveer word vir ander probleme. Hierdie inligting sal met mekaar vergelyk word. Al die proef persone sal dieselfde behandeling ontvang, behalwe vir die twee groepe waar slym verwyder sal word.

Die navorser sal u voor u chirurgie vrae vrae en die antwoorde neerskryf. Hierna sal die navorser bloed by u trek om te toets of the immuun sisteem goed funksioneer. Die trek van die bloed mag pynlik wees en ‘n blou area mag ontwikkel.

Die navorser sal in hierdie studie die volgende rekordeer: resultate van bloed en slym wat getoets word, die temperature van die proef persoon, drukke sal gemeet word, en die resultate van X-strale. ‘n Dokter sal na hierdie resultate kyk om te kyk of die proef persoon ‘n long infeksie ontwikkel. Die resultate van die navorsing sal mediese personeel help om sorg aan pasiënte te verbeter en om mediese onkostes te verminder.

Die navorsingsmetode is goed gekeur deur die etiese komitee van die Gesondhiedswetenskappe van die Universiteit van die Vrystaat. Die navorsing hou nie enige meer gevaar vir die proef persoon in as die buis wat normaalweg gebruik word nie. Proef persone sal gedurende die navorsing noukeurig dop gehou word.

Indien u enige vrae het, is u welkom om my enige iets oor die navorsing of u deelname daaraan, te vra. U mag Mev. M.J.J. Phillips kontak by 082 954 6122 indien u enige vrae het. U naam sal nie in die navorsing saam met u resultate genoem word nie. Alle inligting sal deur die navorser versamel word, in 'n veilige plek gestoor word en nie aan enige ander pesoon sonder u toestemming gegee word nie.

U deelname aan hierdie navorsing is vrywillig en u word nie gevorseer om deel te neem nie. U het die reg om enige tyd te onttrek sonder om enige onregverdige behandeling te ervaar. Daar sal nie enige belonig wees vir die deelname aan die navorsing. Daar sal nie enige fooie betaalbaar wees vir u deelname in hierdie navorsing nie.

Ek, …….. het die toestemming vorm gelees en wil deelneem aan die navorsing uit my eie vrye wil. Ek het 'n kopie van die toestemming vorm ontvang.

…….	**…….**	**……**
Handtekening van deelnemer	**Plek**	**Datum**
…….		**……**
Getuie		**Datum**
…….		**……**
Navorser se handtekening		**Datum**

<u>Toestemming in PROXY</u>

Ek, …… het die toestemming vorm gelees en gee toestemming dat my kind/ eggenoot/ eggenote/ vader/ moeder …….. mag deelneem aan hierdie studie. Ek het 'n kopie van die toestemmings vorm ontvang.

…….	**…….**	**……**
Handtekening	**Plek**	**Datum**
…….		**……**
Getuie		**Datum**
…….		**……**
Navorser se handtekening		**Datum**

<u>Telefoniese toestemming</u>

Die navorser het die toestemming vorm aan my gelees. Ek, ……... …… gee toestemming dat my kind/ eggenoot/ eggenote/ vader/ moeder …… mag deelneem aan hierdie studie. (`n Kopie van die toestemming vorm sal by die besittings van my familie lid geplaas word.)

……	**……..**	**……**
Handtekening van die getuie	**Plek**	**Datum**
……..……..……		**……..**
Navorser se handtekening		**Datum**

4. SOUTH SOTHO CONSENT FORM

(Translators: Sylvia Khoboko and Izél Gerber)

BAKUDI BA BEHILWENG MECHINING E THUSANG HO HEMA BA FUMANENG TSHWAETSO MATSHWAFONG LE DITLAMORAO TSA HO HULWA DIKGOHLELA (SUCTIONING)

Mofuputsi M.J.J. Phillips

Ha mokodi aya epereisheneng e kgolo, peipi e kenywa ka qoqothong ya hae. Peipi ena e hokahangwa le mochini e thusang ho hema. Hona ho thusa mokudi ho hema. Bothata ke hore bakundi ba behwang mechining ena ba fumana tshwaetso matshwafong. Hona ho lelefatsa nako eo mokudi a e nkang mochining le nako eo ae dulang bookelong. Hona ho tla eketsa le tjhelete eo a lokelang ho e lefa. Maemong a kotsi ke hore le mokudi a ka hlokahala (shwa).

Labaka la diphuputso tsena ke ho bona hore na ho na le phapang tshwaetsong ya matshwafo bakuding ba kentsweng di peipi tse fapaneng. Tse ding tsa dipeipi tsena di re dumella hore re ntshe dikgohbla tlase qoqothong. Diphuputso tsena di tshehetswa ka ditjhelete ke Tyco healthcare khamphani e tla thusa ka diphuputso.

Bakudi ba mashome a tsheletseng a metso e tsheletseng ba senang tshwaetso ya matshwafo (e kaba) ba tla nka karolo diphuputsong tsena. Mofuputsi o tla etsa qeto ya hore ke mang ya tla nkang karolo. Bakudi ba tla nkang karolo ba tla arolwa dihlopha tse tharo. Sehlopha sa pele sa bakudi se tla kenywa di peipe tse sebediswang maemong a tlwaelehileng. Dihlopha tse ding tse pedi ditla kenywa dipeipe tse thusang ho ntsha dikgohlola tlase qoqothong.Mokgwa ona o tla sebediswa horeng tse ding le tse ding tse pedi. Bakudi ha ba na ho elellwa taba ena.mokudi ha ana le ho utlwa bohloko. Hona hotla etswa hofihlela peipi e tloswa. Ha mokudi a ka fumana tshwaetso ya matshwafo, o tla shejwa le mathata a mang. Diphuputso tsena di tla bapiswa. Ka ntle ho bakudi ba ntshitsweng dikgohlola, bakudi kaofela ba tla fumana tlhokomelo e tshwanang.

Mofuputsi o tla botsa dipotso mme a ngole fatshe. Kamorao ho moo, mofuputsi o tla hula madi ho sheba hore na masole a mmele a ntse a sbetsa hantle. Hona hoka ba bohloko kapa hwa ba putswa moo madi a ntshitswang teng.

Thutong ena mofuputsi o tla ngola ditlamorao tsa madi le dikgohlela tse ileng tsa tutswa, motjheso wa mokudi, phallo ya madi le ditlamorao tsa dipolata tsa sefuba. Ngaka o tla sheba ditlamorao tsena mme a bolele haeba mokudi ona le tshwaetso ya matshwafo. Ditlamorao tsa diphuputso tsena di tla thusa bahlokomedi ba bakudi ho matlafatsa thlokomelo ya bakudi le ho fokotsa ditefo.

Mokgwa ona wa diphuputso o dumelletswe ke komiti ya lefapha la bophelo bo botle la University ya Foreistata. Thuto ena ha e hlahise bohloko ho mokudi jwalo ka peipi e sebediswang kgafetsa. Bakudi thutong ena ba tla hlokomelwa haholo nakong ya diphuputso.

Ha ona le dipotso o amohetswe hore o ka botsa engkapa eng mabapi le thuto ena. O ka letsa mohala me M.J.J. Phillips ho 082-954-6122 ha ona le dipotso.

Labitso la nao ha le na ho bewa mmoho le ditlamorao diphuputsong tsena. Dintlha tsohle di tla bokellwa ke mofuputsi, a di behe tulong e bolokehileng mme a seke a di arolelena le mang kapa mang kantle ho tumello ya hao.

O karolo thutong ka ho rata ha kao. Ha o qobellwe ho nka karolo mme o na le tokelo ya ho ikgula nako engwe le e ngwe. Ha hona ditefo ho nkeng karolo diphuputsong.

Nna …….. ke badile pampiri ena mme ke itlama ho nka karolo thutong ena. Ke filwe foromo/pampiri e tshwanang le ena.

……..	**……..**	**…….**
Tshaeno	**Tulo**	**Letsatsi la tumellano**
……..		**…….**
Paki		**Letsatsi la tumellano**
…….		**…….**
Lebitso la mofuputsi		**Letsatsi la tumellano**

<u>TUMELLO KA WA LELOKO</u>

Nna …….. ke badile pampiri ena mme ke fana ka tumello hore ngwana waka/monna/mosadi/ntate/mme ……. A ka nka karolo thutong ena. Ke filewe pampiri e tjena.

……..	**…….**	**…….**
Tshaeno	**Tulo**	**Letsatsi la tumellano**
……..		**…….**
Paki		**Letsatsi la tumellano**
…….		**…….**
Lebitso la mofuputsi		**Letsatsi la tumellano**

<u>TUMELLO KA MOHALA</u>

Mofuputsi o mpalletse pampiri ena. Nna …… ke fana ka tumello ya hore ngwana waka/monna/ntate/mme ……. A ka nka karolo thutong ena. (Pampiri e tjena e tla bewa le diphahlo tsa mohaeso).

…….	**…….**	**…….**
Lebitso la Paki	**Boemo mosebetsing**	**Letsatsi la tumellano**
…….		**…….**
Lebitso la mafuputsi		**Letsatsi la tumellano**

5. APPROVAL OF ETHICS COMMITTEE

GESONDHEID
HEALTH

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE

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E-mail address: gndkgcn@med.uovs.ac.za

Mrs G Niemand

27th November 2002

MS MJJ PHILLIPS
ICU
UNIVERSITAS HOSPITAL
BLOEMFONTEIN

Dear Ms Phillips

ETOVS NR 224/02
RESEARCHER: MS MJJ PHILLIPS
PROJECT TITLE: THE EFFECT OF DIFFERENT TYPES OF ENDOTHRACHEAL TUBES ON VENTILATOR-ASSOCIATED PNEUMONIA.

You are hereby informed that the abovementioned study was approved by the Ethics Committee during their meeting held on the 26th November 2002 on condition that the Informed Consent be available in the language the trial person prefers.

Your attention is kindly drawn to the following:

- Failure to submit a progress report not later than one year after approval of the project may result in the termination of the study.
- That all extentions, amendments, serious adverse events, termination of a study etc have to be reported to the Ethics Committee
- These documents have been accepted as complying with the Ethics Standards for Clinical Research based on FDA, ICH GCP and Declaration of Helsinki guidelines
- Translations of the Subject Information Leaflet and Consent Form have to be submitted prior to commencement of a study.

Will you please quote the Etovs number as indicated above in subsequent correspondence, reports and enquiries.

Yours faithfully

For DIRECTOR: MEDICINE ADMINISTRATION

ETHICS COMMITTEE

FOR MEDICAL RESEARCH

ATTENDANCE LIST OF THE MEETING HELD ON THE 29th APRIL 2003

FACULTY MEMBERS (CLINICAL)		
Prof BB Hoek	Chairman M.B. Ch.B. (Pret), M.Med. (Paed.) (UOFS), D.G.G. (UOFS) Department: Paediatrics and Child Health	Present
Prof R Barry	Vice-chairman M.B. Ch.B. (Stell.), M.Med. (Surgery)(UOFS) Department: Surgery	Present
Prof L Goedhals	M.B. Ch.B. (U.C.T.) M.Med (Rad.T.) UOFS Department: Oncotherapy	Absent
Prof MVJ v Vuuren	M.B. Ch.B. (Pret) M. Prax. Med. (Pret) MRCGP (London) Dip. Forensic Med. (SA) Department: Family Medicine	Absent
Prof CS de Vries	MB.Ch.B (UOFS), M.Med Rad.D (UOFS) Department: Diagnostic Radiology	Present
Dr JH van Zyl	MB.CH.B (Pret), Dip. Av Med, M.Med (Internal Medicine) Add. Qualification: Gastro-enterology Dept of Internal Medicine	Present
SCHOOL OF NURSING REPRESENTATIVE		
Prof Y Botma (lady)	B. Soc.Sc (Nursing) Honn, B.Soc.Sc., M. Soc.Sc.. Ph.D. (UFS) School of Nursing	Present
REPRESENTATIVE OF SCHOOL OF ALLIED HEALTH PROFESSIONS		
Ms S van Vuuren (lady)	B. Occupational Therapy (Stell.) Head: School of Allied Health Professions	Present
RELIGIOUS/LAY MEMBER		
Rev D Keta (Coloured)	B.Th. (University of the North) B.Th. (Hons.) (UNISA) Department: Biblical Studies	Present
Mr E Khutsoane	Matric At present: Technical and Logistical assistant Division for the Development Of Student Learning, UOFS	Present

LEGAL MEMBER		
Prof H Oosthuizen	B.Iur., LL.B., LL.D. (UOFS) Department: Criminal Law	Absent
EX OFFICIO MEMBERS (not entitled to vote)		
Dr S Kabane	MB.Ch.B. (Medunsa) Chief Executive Officer Universitas Hospital Bloemfontein	Present
Ms MA Mabandla	Representative Universitas Hospital Bloemfontein	Absent
Mr ST Mohapi	Senior Executive Officer Free State Psychiatric Complex Bloemfontein	Absent
Dr BM Masitha	MB.Ch.B. B.Sc Hons Health Sciences IFE - Nigeria B.Sc NBLS – ROMA H.O.C.S. – Chief Medical officer Free State Psychiatric Complex Bloemfontein	Present
Ms MA Madolo	Senior Executive Officer Pelonomi Hospital Bloemfontein	Absent
Ms NC Sondiyazi	Senior Executive Officer National Hospital Bloemfontein	Absent

For DIRECTOR: MEDICINE ADMINISTRATION
/hs

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Mrs G Niemand

2003-05-05

SR MJJ PHILLIPS
NEUROSURGICAL INTENSIVE CARE UNIT
UNIVERSITAS HOSPITAL
BLOEMFONTEIN

Dear Sr Phillips

ETOVS NR 224/02
RESEARCHER: SR MJJ PHILLIPS
PROJECT TITLE: THE EFFECT OF DIFFERENT TYPES OF ENDOTHRACHEAL TUBES ON VENTILATOR-ASSOCIATED PNEUMONIA.

You are hereby informed that during their meeting on the 29th April 2003 the Ethics Committee approved the following:

- Second blind investigator is now Dr M Spruyt. She is replacing Dr R Krog as he is moving to Nieu Zeeland.
- Auditor: J Abate due to restructuring of management of the sponsor.
- CV's of the two blind investigators
- Consent forms translated into Sotho and Afrikaans.

Your attention is kindly drawn to the following:

- Failure to submit a progress report not later than one year after approval of the project may result in the termination of the study.
- That all extentions, amendments, serious adverse events, termination of a study etc have to be reported to the Ethics Committee
- These documents have been accepted as complying with the Ethics Standards for Clinical Research based on FDA, ICH GCP and Declaration of Helsinki guidelines
- Translations of the Subject Information Leaflet and Consent Form have to be submitted prior to commencement of the study.

Will you please quote the Etovs number as indicated above in subsequent correspondence, reports and enquiries.

Yours faithfully

For DIRECTOR: MEDICINE ADMINISTRATION

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Republiek van Suid-Afrika, Republic of South Africa

ETHICS COMMITTEE

FOR MEDICAL RESEARCH

ATTENDANCE LIST OF THE MEETING HELD ON THE 29th APRIL 2003

FACULTY MEMBERS (CLINICAL)

Prof BB Hoek	Chairman M.B. Ch.B. (Pret), M.Med. (Paed.) (UOFS), D.G.G. (UOFS) Department: Paediatrics and Child Health	Present
Prof R Barry	Vice-chairman M.B. Ch.B. (Stell.), M.Med. (Surgery)(UOFS) Department: Surgery	Present
Prof L Goedhals	M.B. Ch.B. (U.C.T.) M.Med (Rad.T.) UOFS Department: Oncotherapy	Absent
Prof MVJ v Vuuren	M.B. Ch.B. (Pret) M. Prax. Med. (Pret) MRCGP (London) Dip. Forensic Med. (SA) Department: Family Medicine	Absent
Prof CS de Vries	MB.Ch.B (UOFS), M.Med Rad.D (UOFS) Department: Diagnostic Radiology	Present
Dr JH van Zyl	MB.CH.B (Pret), Dip. Av Med, M.Med (Internal Medicine) Add. Qualification: Gastro-enterology Dept of Internal Medicine	Present

SCHOOL OF NURSING REPRESENTATIVE

Prof Y Botma (lady)	B. Soc.Sc (Nursing) Honn, B.Soc.Sc., M. Soc.Sc.. Ph.D. (UFS) School of Nursing	Present

REPRESENTATIVE OF SCHOOL OF ALLIED HEALTH PROFESSIONS

Ms S van Vuuren (lady)	B. Occupational Therapy (Stell.) Head: School of Allied Health Professions	Present

RELIGIOUS/LAY MEMBER

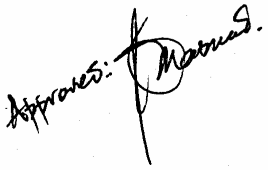
Rev D Keta (Coloured)	B.Th. (University of the North) B.Th. (Hons.) (UNISA) Department: Biblical Studies	Present
Mr E Khutsoane	Matric At present: Technical and Logistical assistant Division for the Development Of Student Learning, UOFS	Present

LEGAL MEMBER		
Prof H Oosthuizen	B.Iur., LL.B., LL.D. (UOFS) Department: Criminal Law	Absent
EX OFFICIO MEMBERS (not entitled to vote)		
Dr S Kabane	MB.Ch.B. (Medunsa) Chief Executive Officer Universitas Hospital Bloemfontein	Present
Ms MA Mabandla	Representative Universitas Hospital Bloemfontein	Absent
Mr ST Mohapi	Senior Executive Officer Free State Psychiatric Complex Bloemfontein	Absent
Dr BM Masitha	MB.Ch.B. B.Sc Hons Health Sciences IFE - Nigeria B.Sc NBLS – ROMA H.O.C.S. – Chief Medical officer Free State Psychiatric Complex Bloemfontein	Present
Ms MA Madolo	Senior Executive Officer Pelonomi Hospital Bloemfontein	Absent
Ms NC Sondiyazi	Senior Executive Officer National Hospital Bloemfontein	Absent

For DIRECTOR: MEDICINE ADMINISTRATION
/hs

Intensive Care
2nd Floor
Universitas Hospital
Universitas
BLOEMFONTEIN
9300

The Medical Superintendent
Universitas Hospital
Private Bag X 20660
BLOEMFONTEIN
9300



Dear Sir or Madam:

Request for approval of performance of Clinical Trial at Universitas Hospital

Hereby I would like request permission to perform a Clinical Trial at Universitas Hospital in the Neurosurgical Unit. The clinical trial form part of the Masters Dissertation I am presently doing at the University of the Free State. Approval has already been obtained from the Expert, Evaluation and the Ethical committee of the Faculty of Health Science.

I am presently employed by Universitas Hospital as a registered nurse as a Training and Developmental officer in the Intensive Care Units.

The development of a ventilator- associated pneumonia in intensive care patients has a detrimental effect of morbidity, mortality and medical cost of the patient and the institution.

The **purpose** of the clinical trail is to determine the effect of three endotracheal tubes on ventilator-associated pneumonia. The research **objectives** are to compare three groups of subjects intubated with different types of endotracheal tubes regarding the incidence of ventilator-associated pneumonia, causative organisms, length of intensive care stay, cuff pressures, morbidity and mortality.

Sixty-six candidates undergoing neurosurgery admitted in the neurosurgical intensive care and receiving mechanical ventilation, will be studied according to the objectives above-mentioned. The company sponsoring the clinical trial is Tyco Health Care. The company will supply the endotracheal tubes, disposable ventilator circuits, bacterial filters and closed system suctioning catheters. They are also responsible for monitoring and auditing the data of the research. The patient and the institution will therefor benefit from the research. For more detail about the research, see the protocol attached.

I trust that my request receives your favorable consideration.

Yours truly,

Maria Phillips

FREE STATE PROVINCIAL GOVERNMENT

Health

Dr S Kabane, Chief Executive Officer, Universitas Hospital, Private Bag X20660, Bloemfontein 9300
Tel (051) 4053556, Fax (051) 4440792, Sel: 083 441 3910, E-mail: kabans@doh.ofs.gov.za

Ms M Phillips
Intensive Care
2nd Floor
Universitas Hospital
BLOEMFONTEIN

REQUEST FOR APPROVAL OF PERFORMANCE OF CLINICAL TRIAL AT UNIVERSITAS HOSPITAL

Your request to performance a clinical trial at Universitas Hospital is relevant.

Approval is hereby granted for you to perform this trial in the Neurosurgical Unit at Universitas Hospital to determine the effect of three endotracheal tubes on ventilator-associated pneumonia.

Yours faithfully

DR S KABANE
CHIEF EXECUTIVE OFFICER:
ACADEMIC HEALTH COMPLEX

DATE: 3 December 2002
vdva:gk5421

S. KABANE
03 DEC 2002
C.E.O.

A Healthy & self-reliant
Free State Community