EFFECTS OF HUMIDIFIED GAS INSUFFLATION IN ENDOSCOPIC SURGERY

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by

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Abstract

Three studies were performed to evaluate the effects of humidified gas insufflation in endoscopic surgery.

A first experimental study evaluated whether humidification of warmed insufflated carbon dioxide (CO_2) gas during laparoscopic procedures would resolve the problem of laparoscopy-induced hypothermia. After insufflation with cool dry gas, core temperature dropped significantly more than experienced by control animals and those insufflated with heated humidified gas. These data confirm that the majority of heat lost during laparoscopic insufflation is due to water evaporation, and this can be prevented by using heated and humidified insufflation gas.

Secondly a randomised controlled clinical trial conducted during laparoscopic cholecystectomy was performed to determine the extent of heat preservation and postoperative pain reduction using humidified CO_2 gas insufflation instead of standard dry insufflation gas. There was no significant difference in core body temperature between the two groups for this brief operation. Pain assessed by the Analogue Pain Score was significantly reduced in the group following humidified gas insufflation compared to the control group. The humidification of gas insufflated during laparoscopy therefore can reduce the degree of postoperative hypothermia and may result in less peritoneal reaction and less postoperative pain.

A third study was designed to determine whether these beneficial effects of humidified gas insufflation applied also to thoracoscopy. The recorded fall in core body temperature after humidified gas insufflation was significantly less than the fall following insufflation of dry gas, and also significantly less than the temperature drop when no gas was insufflated. Electron microscopic examination revealed that the pleural surface sustained ultrastructural destruction of microvilli only when standard dry gas was insufflated. It is concluded that the potential benefits of humidifying insufflation gas during thoracoscopy warrant its evaluation in the clinical setting.

To summarise, it is concluded that the insufflation of humidified gas during laparoscopy and thoracoscopy may have a body temperature preserving as well as a post-operative pain reducing effect. Ultrastructural imaging suggests that physical trauma of peritoneum and pleura is less when humidified gas is insufflated rather than dry gas. No adverse effects of humidified gas insufflation were seen.

Declaration

I declare that this thesis contains no material which has been accepted for the award of any other degree or diploma in any University and that to the best of my knowledge and belief, the thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis. I further consent to the thesis being made available for photocopying and loan if applicable, if accepted for the award of the degree.

Wolfgang Mouton

Preface

Part of the work described in this thesis has been accepted or submitted for publication. These publications are listed in the order they were submitted.

1. Mouton WG, Bessell JR, Millard SH, Baxter PS, Maddern GJ.
   A randomised controlled trial assessing the benefit of humidified insufflation gas during laparoscopic surgery.
   Surgical Endoscopy, in press.

2. Mouton WG, Bessell JR, Pfitzner J, Dymock RB, Brealey J, Maddern GJ.
   A randomised controlled trial to determine the effect of humidified carbon dioxide insufflation during thoracoscopy.
   Surgical Endoscopy, in press.

3. Mouton WG, Bessell JR, Maddern GJ.
   Looking back to the advent of modern endoscopy - the 150th birthday of Maximilian Nitze .
   World Journal of Surgery, in press

4. Mouton WG, Bessell JR, Maddern GJ.
   Pain after laparoscopy.
   Surgical Endoscopy, in press.

5. Mouton WG, Pfitzner J, Bessell JR, Maddern GJ
   Anaesthetic death during single-lung ventilation in pigs.
   British Journal of Anaesthesia, submitted

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The studies described involved the Department of Surgery at the Queen Elizabeth Hospital, University of Adelaide.

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The start in the new field of research following the clinical years was facilitated by the assistance, advice and encouragement of Mr Justin R Bessell. He also improved my articles with his delightful English.

Dr John Pfitzner, deputy Head of the Department of Anaesthesia, has one of his main interests in the field of Thoracic Surgical Anaesthesia and performed the demanding task of giving anaesthesia in experimental thoracoscopic surgery. He is a perfectionist and his help was invaluable in the articles concerning physiology, pathophysiology and anaesthetic aspects.

Mrs Sue H Millard was a tremendous help in technical and instrumental matters.

Mrs Paula S Vanderzon-Baxter was very supportive in the clinical studies and in linguistic and administrative work.

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My wife Kim gave wings to this work with her esprit and with excellent ideas which lead to many improvements.

SECTION 1 AIMS

The thesis attempts to answer the following questions :

What is the ideal experimental setting in which to study humidified gas insufflation ?

Is humidified gas insufflation during laparoscopy technically possible in the operating theatre environment ?

What is involved in the construction of a laparoscopic humidifying system ?

What are the thermodynamics of such a system, and does it permit heat preservation by the subject ?

Is there a core temperature difference at the end of an operation using humidified compared to standard gas insufflation, and if so do the experimental results conform to theoretical thermodynamic calculations ?

Is the clinical use of humidified gas safe ?

Is operative visibility impaired during humidified gas insufflation ?

Are there effects on blood coagulation following the use of humidified gas insufflation ?

What is the effect of humidified gas insufflation on postoperative pain and for how long would such an effect last ?

Are there subgroups of the population that would benefit preferentially from humidified gas insufflation ?

What are the ultrastructural effects of humidified gas insufflation on exposed membranes ?

What mechanism can be postulated to explain any observed ultrastructural changes to exposed membranes from humidified gas insufflation ?

What are the final conclusions ?

SECTION 2 INTRODUCTION

2.1. HISTORY OF ENDOSCOPY

It was Hippocrates (460-375 BC) of the Greek island of Kos, who first described the endoscopic examination of the rectum with the use of a speculum similar to the instruments in use today (Lau et al 1997). Subsequently various specula have been discovered in the ruins of Pompei (79AD), which were once used for vaginal, cervical, rectal, nasal and ear inspection (Figure 1).

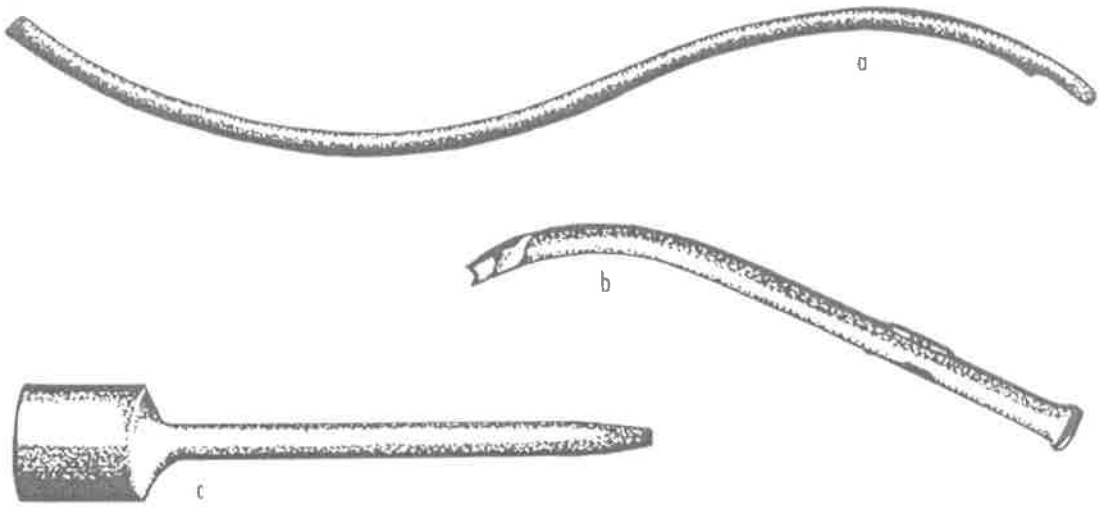

Figure 1 Catheter and speculum from the surgeon's house of Pompei, 79 AD

In 1805 Philippe Bozzini, in Frankfurt am Main, was the first person to use an artificial light source to inspect the bladder (Bozzini 1806), and in 1868 Bevan removed foreign bodies from the oesophagus with the aid of an oesophagoscope (Bevan 1868). In the following year, Pantaleoni was able to remove a common cause for postmenopausal bleeding - an intrauterine polyp - and cauterise it with silver nitrate (Pantaleoni 1869). In 1870 Kussmaul was able to inspect the stomach of a professional sword swallower using a rigid tube (Marguelies and Shabot 1993).

Endoscopy received two revolutionary improvements when Maximilian Nitze (Figure 2) realised firstly that the field of view during endoscopy could be enlarged by the use of an optical system and secondly that the light source should be placed on the tip of the instrument (Rathert 1967). Nitze presented a such designed and much improved cystoscope in 1877 (Figure 3).

Figure 2 Maximilian Nitze (1848-1906)

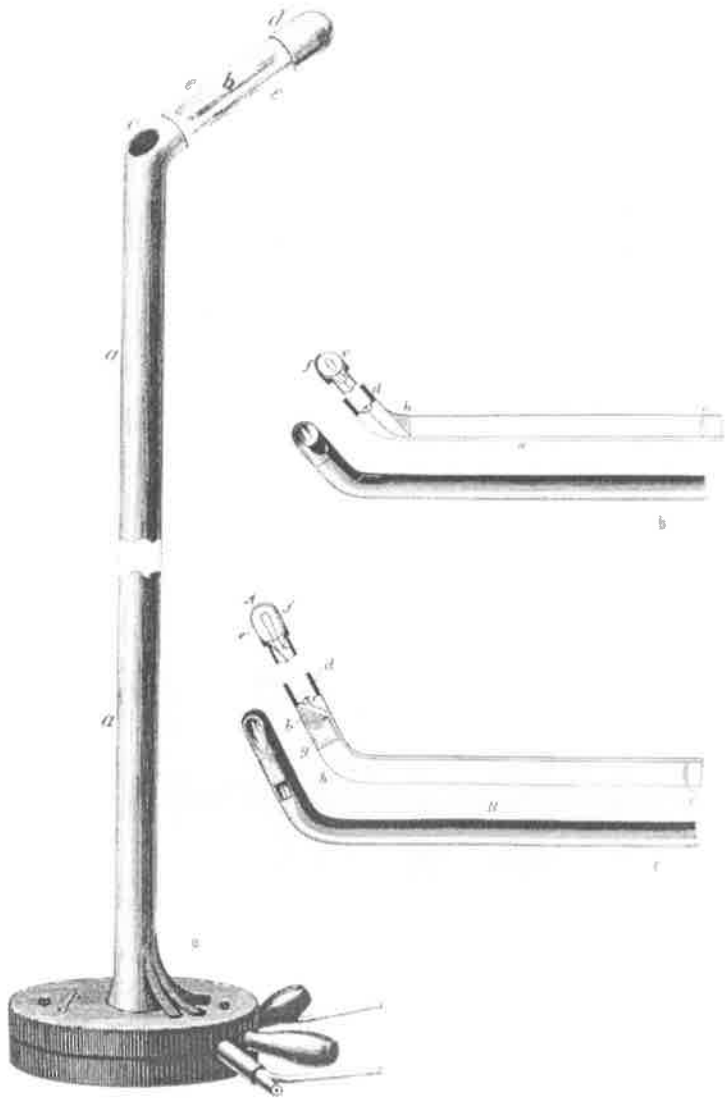

Figure 3 Cystoscope of Maximilian Nitze, 1877

Light source improvements followed with the invention of the incandescent light bulb by Edison in 1879. The following year Johann von Mikulicz constructed a gastroscope that could be angled at its lower third by up to 30 degrees (Rosin 1993). Kilian, in 1898, constructed and successfully used the first bronchoscope (Marguelies and Shoabot 1993).

In 1910 Hans Christian Jacobeus (Figure 4), the Professor of Medicine - not Surgery! - in Stockholm, used a cystoscope (Figure 5) to perform the first thoracoscopy and later on during the year used the same instrument for the first endoscopically guided laparoscopy (Thomas, 1994). In the following years he utilised this thoracoscopic technique to divide pleural adhesions (Thomas, 1994).

Figure 4 Hans Christian Jacobaeus with assistant

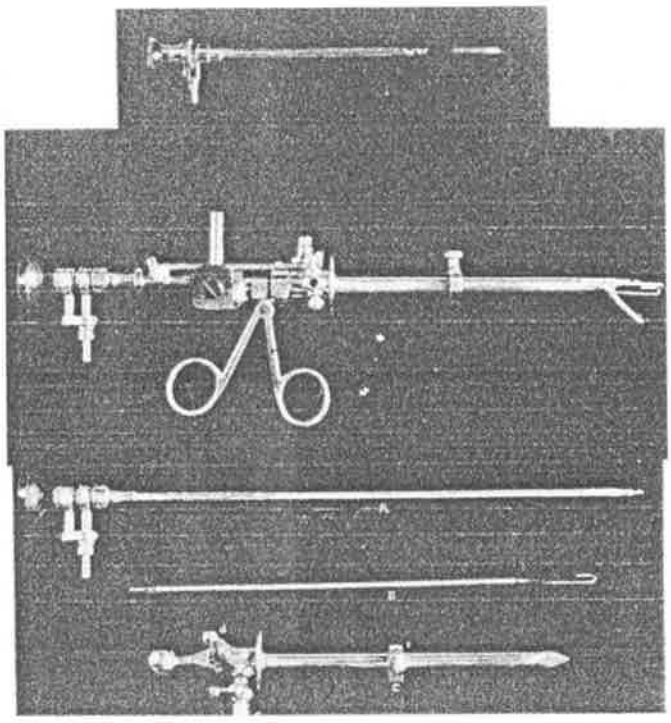

Figure 5 Cystoscope of Hans Christian Jacobaeus used for thoraco- and laparoscopy

The pneumoperitoneum has been used to perform much visually improved laparoscopies since 1918 (Goetze, 1918). The more rapidly absorbed carbon dioxide gas was first used as insufflating gas by Zollikofer in 1924 (Zollikofer 1924). In 1930, Lemm demonstrated that bundled threads of fiber glass can act as flexible endoscopic optical systems (Fourestier 1962), however this idea was not utilised in the endoscopic world for another 24 years (Rosin 1993). Operative endoscopy in the abdomen began in 1933 when Fervers performed laparoscopic adhesiolysis (Gotz, 1993). Boesch, in 1936, performed the first laparoscopic tubal ligation using the application of monopolar electrocoagulation to the fallopian tubes (Boesch 1936). In the same years the first semiflexible gastroscope was designed containing 48 lenses at 77cm length (Lau et al ,1997). In 1938 , Veress described a spring-loaded needle with an inner stylet that automatically converted the sharp cutting edge to a rounded end incorporating a side hole. It was created to perform safe thoracoscopies. Hopkins, in 1952, introduced a rod-lens system consisting of air lenses and long glass spaces and applied two years later fiber glass technology to the endoscope. This resulted, a further three years later, in the first functional fiberoptic instrument by Hirschowitz (Rosin, 1993).

Kurt Semm introduced the automatic insufflation device in 1963. He also introduced many gynaecological procedures to laparoscopic surgery; as well as performing the first laparoscopic appendectomy 1982 (Lau et al ,1997).
In 1986 a further technical improvement in the form of the computer chip camera was developed and in 1987 the first laparoscopic cholecystectomy was performed by Mouret in Lyon (Filipi et al, 1991). This event was the primary stimulus in the

subsequent development of operative laparoscopy on a rapidly expanding number of organs within the thorax and abdomen.

2.1.1. MAXIMILIAN NITZE

1998 marks the 150th anniversary of the birthday of Maximilian Nitze (1848-1906), a German scientist responsible for the initiation of modern endoscopy by integrating two of his ideas in the construction of the first functional cystoscope. Nitze realised that the field of view during endoscopy could be enlarged by the use of an optical system, and that the light source should be placed on the tip of the instrument. He presented this cystoscope on the 2nd of October 1877 for the first time, at the age of 28 years.

Maximilian Nitze (Figure 2) was born in 1848 in Berlin and died at the age of 57 years in the same city (Rathert, 1967). Nitze is characterised as a man of highest academic profile. He lived a somewhat withdrawn life, being a shy man who lived alone, and reportedly did not care much for society or politics (Reuter and Reuter, 1988).

Nitze commenced his medical studies at the University of Heidelberg, completing his education in 1874 at Würzburg and Leipzig. After finishing his military service he worked as an "Assistent" at various hospitals in Dresden, the most important of which in terms of his future career, being the "Stadtkrankenhaus Dresden-Friedrichstadt" hospital. Here he became inspired by the work of Julius Bruck, a dentist, who performed diaphanoscopy of the bladder by inserting an incandescent, water-cooled platinum wire in the rectum (Rathert, 1967; Reuter and Reuter, 1988). The illumination of the bladder was however insufficient and the rectum was

unfortunately burned in some cases. Attempts to examine the interior of the bladder were not new however, having been undertaken first by Bozzini in 1807 using a reflected candle light source, which had also proven to be an insufficient light source, and furthermore was too painful for patients due to the size of the instrument (Davis, 1992; Lau et al, 1997).

Nitze was inspired to improve the view whilst one day cleaning the dusty eye piece of his microscope he checked it to be clear by looking across at the Matthaei Church (Reuter and Reuter, 1988). Suddenly he realised that the image problems could be solved by enlarging the field of view with an optical system. Shortly thereafter he recognised that the light source had to be placed at the tip of the instrument in the same way that "to light up a room one must carry the lamp inside" (Hausmann, 1987; Wehnert, 1979).

Under Nitze's instructions a 21 French instrument illuminated by a water-cooled platinum wire was built by technicians Wilhelm Deicke and Louis Beneche, the opticians of the University of Berlin. On October the 2nd 1877 Nitze presented his cystoscope for the first time at the age of 28 years to the National Medical College (Hausmann, 1987) at the Pathological Institute of the Friedrichstadt Hospital in Dresden .

To improve the instrument further Nitze moved to Vienna in 1878 to avail himself of more sophisticated technical expertise and constructed optimised versions of the cystoscope with instrument maker Joseph Leiter (Rathert, 1967). In 1880 Nitze

moved home to Berlin after quarrels with Leiter, who tried to claim the cystoscope as his own work by asserting "the microscope and the rifle are named after their designers and not after the inventors of the ideas" (Reuter and Reuter, 1988). Back in Berlin, Nitze founded the first private Urology Hospital. Thomas Edison's invention of the incandescent light bulb in 1879 allowed further improvements to be made to the apparatus. By 1887 Nitze had developed a cystoscope that no longer needing a water cooling system. His cystoscopic observations were sufficiently comprehensive to be published in 1889 in the "Textbook of Cystoscopy", and at the turn of the century he became Professor at the University of Berlin. He improved his instruments further and was the first person to take endoscopic photographs and to use movable loops for operations inside the bladder. Shortly after finishing the second edition of his textbook in 1906 Nitze died, following two cerebro-vascular accidents at the age of 57 years.

Nitze's invention heralded the advent of modern endoscopy. He was responsible for the emergence of the speciality of Urology and anticipated the potential widespread use of endoscopy by formulating the patent of his invention as an "apparatus for direct illumination and investigation of human and animal hollow organs" (patent number 6853 dated 7th February 1879).

Within four years of his death such farsightedness proved well-founded, when in 1910 Christian Jacobaeus, the Professor of Medicine (not Surgery) in Stockholm used the Nitze cystoscope to perform the first thoracoscopy and later during the

same year the first endoscope-guided laparoscopy (Braimbridge,1993; Thomas, 1994).

2.2. ENDOSCOPY RELATED MORBIDITY AND PROPHYLAXIS

The morbidity related to endoscopic surgery incorporates the morbidity involved with any general surgical procedure. Of these, wound infection and incisional hernia formation are worth mentioning.

Port site infection is reported with an incidence of 0.12% for laparoscopic hernia repair (Philips et al, 1995), 1% for laparoscopic cholecystectomies and 3% for laparoscopic appendectomies (Crist and Gadacz, 1993).The usual sterile techniques are mandatory. The retrieval of a potentially infected specimen or a specimen known to be infected is performed via the use of a sterile bag in which the specimen is placed during the retrieval, thus minimising the risk of port site infection.

The incidence of port site incisional hernia formation has been reported as 0.1% (Crist and Gadacz, 1993; Philips, 1995). Other complications are specific for endoscopic procedures and are discussed in the text to follow.

2.2.1. NEEDLE AND TROCAR INJURY

The most commonly occurring needle and trocar injuries are those involving vascular structures and viscera. In a group of 100,000 gynaecological procedures

(Mintz, 1977) and in 3,229 laparoscopic herniorrhaphies (Philips et al ,1995) major retroperitoneal vascular injury is reported with an incidence of 0.03% . The mortality rate related to such injuries is significant, ranging between 9 and 13% (Baadsgaard et al, 1989; Deziel et al, 1993). Minor injuries predominantely involve the epigastric vessels. .Most commonly injured viscera are bowel and bladder with a reported incidence of 0.1% (Deziel et al, 1993; Philips et al, 1995).

Several techniques have been suggested to prevent such needle and trocar injuries. One of these is the cut-down technique whereby a blunt tipped Hasson cannula is placed under direct vision (Hasson, 1971). A further option is the placement of an insufflation needle with visual control (Schaller et al, 1995). A variety of similar techniques also exist (Melzer, 1995). Depending on the type of endoscopic surgery, visceral injury may also be prevented by the insertion of a nasogastric tube or urinary catheter.

2.2.2. PATHOPHYSIOLOGY OF PNEUMOPERITONEUM

The tension pneumoperitoneum is known to potentially cause a variety of cardio-respiratory complications. Arrhythmias, impaired respiratory function and alterations in venous return and cardiac output are documented (Ishizaki et al, 1993). The potential also exists for the development of a pneumothorax, pneumomediastinum, pneumopericardium or gas embolism, although these complications are fortunately rare (Baxter and O'Dwyer, 1995).

The risk of thromboembolic phenomena may also be increased as compared to open surgery due to the elevated pressure placed on the splanchnic venous system. Based on these potential complications it is recommended that lower insufflation pressures are used. It is also recommended that deep vein thrombosis prophylactic measures, such as compression stockings, intermittent calf compression devices, and the administration of low molecular weight heparin pre-operatively be incorporated into laparoscopic procedure protocols.

2.2.3. PORT SITE METASTASIS

As laparoscopy is increasingly used to perform tumor resections, the phenomenon of port site metastasis has been noted to be a significant complication (Jakub and

Greene, 1998; Wexner and Cohan, 1995). The exact pathophysiology of port site metastasis is still not known. Port site metastases have been described to occur following surgery for the gallbladder, colon, pancreas, stomach, lymph nodes and gynaecological procedures. Port site metastases have even been observed after the apparently curative laparoscopic resection of early stage tumors (Gleeson et al, 1993; Lauroy et al,1994). The incidence of port site metastasis was reported by Ramos in 208 laparoscopic colectomies as 1.44% at the end of one year of follow-up. It was reported as 0.48% when diffuse peritoneal carcinomatosis was not present (Ramos et al, 1994). A further study revealed a 6.3% incidence of port site metastasis in the three years following laparoscopic cancer surgery in 33 patients (Seiler, 1995). The retrieval of the specimen via an endobag does not ensure the prevention of this phenomenon, and indeed port site metastases have been shown to occur in ports not involved with specimen retrieval (Wexner and Cohan, 1995). There is a concern that pneumoperitoneum may aid in metastatic spread. This is founded on the observation that pneumoperitoneum causes capillary stasis and therefore may favour metastatic implantation of circulating cells. Tumor cells may be also spread by aerosolisation caused by sudden loss of pneumo-peritoneum. This may occur when laparoscopic ports are dislodged at the exchange of instruments, or when deliberate venting of cautery smoke is performed. Tumor cells may be also spread by directly driving malignant cells into lymphatic and vascular systems under pressure (Jakub and Greene, 1998). It is also not known at this stage whether the incidence of port site metastasis is higher than the incidence of metastasis in incisions following open procedures inspite attempted comparisons (Jakub and Greene, 1998). Port site metastasis after laparoscopic surgery remains a

topic of intensive ongoing research and long-term follow-up studies and results are needed. At this stage, the only way to prevent port site metastasis is to limit the use of laparoscopy to palliative resections and the treatment of benign disease (Ramos et al, 1994).

2.2.4. PAIN

Post-operative pain after laparoscopy is often significant. Up to 80% of patients require opioid analgesia following laparoscopic surgery (Madsen and Jensen, 1992). Postoperative pain reduction, reduced length of hospital stay and faster recovery times are therefore central topics of improvement for laparoscopy patients. Factors influencing pain during endoscopy are discussed in detail in section 2.3.

2.2.5. HYPOTHERMIA

Considering the clinical implications of side effects from perioperative hypothermia, core temperature changes and core temperature influencing factors during laparoscopy are of great interest. This topic together with a special focus on factors influencing the core temperature are discussed in detail in section 2.4.

2.3. FACTORS INFLUENCING PAIN DURING ENDOSCOPY

2.3.1. INTRODUCTION

Laparoscopy is a credible alternative to open surgery for a range of procedures in various surgical specialities. For many but not all of these procedures laparoscopic surgery has displayed advantages over open surgery including lower morbidity and mortality, smaller incisions, reduced length of hospital stay, faster recovery and earlier return to normal activities and work (Baxter and O'Dwyer, 1995; Berggren et al, 1994; Bessell et al, 1996; Ellstrom et al, 1996; Glaser et al, 1995; Goodale et al, 1993; Grace et al, 1991; Jakeways et al, 1994; Maddern et al, 1994; Neugebauer et al, 1991; Pier et al, 1994).

From the patient's perspective, reduced postoperative pain is one of greatest advantages of laparoscopic compared with open surgery (Baxter and O'Dwyer, 1995; Berggren et al, 1994; Cunningham and Brull, 1993; Dallemagne et al, 1991; Grace et al, 1991; McMahon et al, 1993; Ortega et al, 1995; Stage et al, 1997). However, pain is not completely abolished following laparoscopy. Patients frequently describe subdiaphragmatic and shoulder tip pain (Korell et al, 1996; Murat et al, 1996; Pier et al, 1994; Stage et al, 1997), in addition to the discomfort of port-site incisions. Some authors report that 80% of patients require opioid analgesia following laparoscopic surgery (Madsen and Jensen, 1992).

There are several reasons why there is still room for surgeons to improve management of post-laparoscopy pain. Firstly, better pain control would magnify the other advantages of laparoscopy in terms of earlier discharge and recovery time. Secondly, surgeons may enjoy the satisfaction of the reduced levels of postoperative pain by comparison with their former experiences with open surgery, and not identify pain as an issue that needs further attention. Thirdly, it is commonly believed that reduced postoperative pain following laparoscopy emanates from the smaller size of the incisions, when there is evidence to suggest that the dominant source of pain and discomfort following laparoscopy is from the peritoneum rather than the skin or abdominal wall (Helvacioglu and Weis, 1992). Finally, the surgeon's perception of post-laparoscopy pain may be masked by the current tendency for the patient to be discharged rapidly following a reduced hospital admission.

The aetiology of post-laparoscopy pain is multifactorial, and treatment of any one factor in isolation may not achieve the desired result. However the surgeon is in a unique position to influence many of the putative causes by relatively minor changes in technique, with a correspondingly additive improvement in outcome. A concise knowledge of the multi-factorial aetiology of post-laparoscopy pain and how the impact of each contributing factor might be nullified will assist this process.

In the following chapters I will discuss the aetiology and the treatment of post-laparoscopy pain :

2.3.2. FACTORS ASSOCIATED WITH GASEOUS PNEUMOPERITONEUM

2.3.2.1. Neuropraxia of the phrenic nerves during gas insufflation

To allow sufficient access space for operative manoeuvres most surgeons still initiate a pneumoperitoneum during laparoscopic procedures. To avoid the complications of the abdominal compartment syndrome insufflation pressure is usually kept below 15 mmHg, which still allows sufficient exposure (Alexander and Hull, 1987; Bessell and Maddern, 1998; Cunningham and Brull, 1993).

It has been suggested that distension of the diaphragm and the resultant phrenic nerve neuropraxia possibly contribute to postoperative pain, which may include the related C4 dermatome (Coventry, 1995; Korell et al, 1996; Pier et al, 1994). A 20% stretch of the nerve results in complete occlusion of the endoneural vessels and total ischaemia of the nerve (Tiel and Kline, 1996). Yet in a prospective randomised study insufflation pressures above 18 mmHg did not show a significant difference in pain and analgesic consumption compared to pressures as low as 9 mmHg (Pier et al, 1994).

It is likely that pressure peaks have a greater noxious influence on the phrenic nerves than the plateau pressure of the pneumoperitoneum. It is believed that the more time the nerve has to adapt to the stretch, the less likely it is that distension injury will occur. Tissue damage by combustion is an additional mechanism that has been reported to damage the phrenic nerves (Waleczek et al, 1993).

The use of subdiaphragmatically administered local anaesthetics especially those with long acting effects such as bupivacaine, are recommended in several studies (Narchi et al, 1991; Weber et al, 1997). Although the risk of local anaesthetic toxicity exists, with appropriate dosage precautions this has been shown to be quite safe (Helvacioglu and Weis, 1992).

2.3.2.2. The type of insufflated gas and intra-abdominal pH

The phrenic nerves may be damaged by the acidic milieu created by the dissolution of CO_2. The intraperitoneal pH when CO_2 gas is insufflated has been measured at

6.0 immediately postoperatively. On the first postoperative day this rises to 6.4-6.7, on the second postoperative day to 6.8-6.9 and thereafter normalises to above 7.0 (Pier et al, 1994). Similar values were found when argon gas was substituted (Pier et al, 1994). In the past N_2O was thought to be less irritative (Sharp et al, 1982), but its side effects and explosive nature have placed major limitations on its use. Potential neural injury to the phrenic nerves by the acidic milieu may be minimised by a shorter duration of exposure to the implicated gases.

2.3.2.3. Residual intra-abdominal gas

Several reports have indicated that residual intra-abdominal gas post laparoscopy causes pain (Alexander and Hull, 1987; Fredman et al, 1994). Carbon dioxide dissolution, intra-abdominal acidosis and the consequent peritoneal irritation occur for a longer period if the gas is not evacuated at the end of a laparoscopic procedure. Residual gas may also result in a loss of peritoneal surface tension and support to abdominal viscera and so contribute to postoperative pain (Alexander and Hull, 1987). A gas-draining catheter has been utilised for the first six postoperative hours allowing visceral peristaltic and voluntary abdominal muscle activity to expel

residual gas (Alexander and Hull, 1987). Patients with a gas drain in-situ were reported to have significantly less pain after the operation than a control group without such a drain.

The irritative effect of wound drains could potentially negate any advantage conferred by expulsion of residual gas by this mechanism. A separate study reported significantly less postoperative pain when residual gas was actively aspirated at the completion of laparoscopic cholecystectomy without the use of a drain as compared to patients in whom no active aspiration was undertaken (Fredman et al, 1994). It is therefore suggested that intraperitoneal gas be actively evacuated at the end of the laparoscopic procedure by instrumental suction under direct vision.

2.3.2.4. Temperature of gas

The effect of gas temperature on postoperative pain after gynaecological laparoscopic procedures has been investigated in a prospective randomised study of standard insufflation gas (20°C) versus gas at body temperature. This study found that there was a significant reduction of pain in those patients where warmed gas

was used, especially with respect to diaphragmatic and shoulder-tip pain, with a lasting effect of three days (Pier et al, 1994).

In another prospective randomised study of 103 patients significant pain reduction was observed in patients receiving body temperature insufflation gas (CO_2) compared to the patients having standard gas insufflated (Korell et al, 1996). However, rigorously controlled animal studies have determined that the physiological impact of warm gas insufflation is minimal (Bessell and Maddern, 1998). These have experimentally confirmed the theoretical principles of thermodynamics which indicate that considerably more heat expenditure from the patient is needed to evaporate body water to humidify the initially dry CO_2 stream, than is required to heat the initially cool CO_2 gas to body temperature. In these energy calculations, the component attributable to heating the insufflated CO_2 to physiological levels can be ignored because of the extremely low specific heat of the gas. Because it takes so little energy to heat gas insufflated at room temperature, it almost instantaneously reaches body temperature in the abdomen. It is therefore hard to imagine how this phenomenon could influence postoperative pain.

2.3.2.5. Humidity of gas

The role of humidification of the insufflated gas on pain has not been investigated so far. However, insufflation of humidified gas appears more physiological than insufflation of dry gas during endoscopy. Having presumed a possible greater physical trauma to exposed membranes using dry gas insufflation ascompared to humidified gas insufflation, can we expect more postoperative pain when dry is insufflated rather than humidified gas ?

2.3.2.6. Gasless laparoscopy

Perhaps the most intriguing opportunity to absolve the pain resultant from gas insufflation is the use of gasless laparoscopy. The use of retractor systems permits laparoscopic exposure without the creation of a pneumoperitoneum.

Another major advantage of gasless laparoscopy is that it abolishes the requirement for elevated intra-abdominal pressure and by doing so diminishes the risk of thromboembolic and cardiopulmonary complications associated with the abdominal compartment syndrome. The disadvantages are that some of these devices require additional small incisions which may potentiate pain from abdominal wall and peritoneal trauma. The net effect on post-laparoscopy pain remains to be evaluated.

Device assembly can sometimes be complicated and the operative exposure is somewhat different than that provided by CO_2 insufflation.

Gasless laparoscopy may be of advantage if pneumoperitoneum is contraindicated for cardiopulmonary reasons. If only standard gas insufflation is available, gasless laparoscopy may reduce insufflation-induced pain but at the risk of some additional trauma.

2.3.3. OPERATIVE FACTORS

2.3.3.1. Wound pain

The number and size of the incisions used vary between different procedures and also between different centres. When laparoscopy is used to facilitate major resectional surgery (splenectomy, colectomy) larger incisions may be necessary to deliver major specimens, and wound pain may become clinically relevant.

Local anaesthesia, preferably administered into the incision of access before the wound is created is recommended by many authors with significant pain reduction in both open (Gibbs et al, 1988; Wright, 1993) and laparoscopic procedures (Murat et al, 1996). Not all studies have shown a significant difference however (Adams et al,

1991; Coventry, 1995; Gibbs et al, 1988).

For laparoscopic procedures only small amounts of local anaesthetics will be required, side effects are anticipated to be minimal, and the use of local anaesthesia is recommended.

2.3.3.2. Wound drainage

Wound drains after laparoscopic surgery are usually sited on the lateral aspect of the abdomen, traversing muscle layers. The umbilical incision is less commonly used due to a greater incidence of pain, infection and potential incisional herniation at this site if the defect is not formally closed.

Active movements of the patient and respiratory excursion can provoke or increase pain caused by wound drains. It is recommended that the necessity for wound drainage be carefully individualised, rather than insertion as a routine.

2.3.4. ANAESTHETIC FACTORS

The use of non-steroidal anti-inflammatory drugs after induction of anaesthesia is recommended during laparoscopic procedures (Coventry, 1995). The direct

analgesic effect is not sufficient for their use as single agents, however they have a useful opioid-sparing and anti-inflammatory effect especially when combined with paracetamol. In several studies ibuprofen was found to be a useful alternative to fentanyl for providing postoperative analgesia in outpatient surgery with a significant reduction in postoperative pain and nausea (Rosenblum et al, 1991; Smith et al, 1993).

2.3.5. SOCIO-CULTURAL FACTORS

The socio-cultural environment affects hospital stay and recovery time. This variable, encountered on almost a daily basis by all practising surgeons, was well demonstrated in a study comparing the course after laparoscopic cholecystectomy in French and American patients. Postoperative discomfort had resolved within 2 weeks in 73% of the French and in 93% of the Americans. A higher percentage of Americans returned back to work in a given time period than the French patients (Vitale et al, 1991).

It is accepted that despite adhering to principles of best practice, a multitude of factors including previous pain experiences and individual thresholds will influence postoperative pain perception and recovery time.

2.3.6. SUMMARY

Based on the literature available, several recommendations can be made in an attempt to minimise pain after laparoscopic surgery. First, the surgeon should take a moment to consider the socio-cultural and individual factors likely to influence the pain experience for each patient, and discuss the likely outcome as part of the informed consent process. In the operating room, it is recommended that port site wounds be injected with local anaesthetic before any wound is created. Thereafter the intra-abdominal pressure during insufflation should be kept below 15 mmHg and unnecessary pressure peaks and prolonged insufflation avoided. Gasless laparoscopy may reduce insufflation-induced pain but at the risk of additional trauma caused by additional incisions and by mechanical traction. Whilst under anaesthesia a non-steroidal anti-inflammatory agent should be administered. At the end of the operation the surgeon should try to evacuate the intraperitoneal gas under direct vision. Finally wound drainage should be carefully individualised and not be inserted as a routine.

2.4. FACTORS INFLUENCING CORE TEMPERATURE DURING ENDOSCOPY

2.4.1. FACTORS UNRELATED TO INSUFFLATION

Several surgical and anaesthetic factors have been implicated in the reduction of core body temperature during surgical procedures. Respiratory heat loss is relatively small (Bickler and Sessler, 1990) and as there is only a minimal reduction in heat protection during anaesthesia, the predominant mode of heat loss during surgical procedures is via cutaneous mechanisms. Several factors contribute to this cutaneous heat loss including the undressed, immobile patient lying exposed to the cool theatre environment (Morris and Wilkey, 1970), evaporative losses occurring from surgical incisions and from skin preparation solutions and the use of cold irrigation fluids (Imrie and Hall, 1991). In addition, surgical incisions as in laparotomy and thoracotomy provide an increased surface area for heat losses to occur (Morris and Kumar, 1972; Roe, 1971; Tollofsud et al, 1984).

A minimal to moderate drop of the core body temperature is usually well tolerated. Larger temperature reductions can result in clinical hypothermia , defined as a core temperature below 36^0C (Morris and Kumar , 1972). The clinical implications of

perioperative hypothermia are evident when its potential side effects are considered. Amongst those side effects reported are impaired myocardial function (Mattheussen et al, 1990), respiratory depression, negative nitrogen balance (Carli et al, 1989) increased susceptibility to dermal infection (Sheffield et al, 1994), induction of a hypokalaemic state (Boelhouver et al, 1987; Laszlo et al, 1990) , thrombocytopenia, and depletion of clotting factors (Ellis et al, 1957) .

A significant adverse effect on the mortality rate has been reported amongst patients suffering from perioperative hypothermia. In one study, the mortality rate amongst normothermic postoperative patients was 4% , with this figure rising dramatically to 24% amongst postoperative patients who remained hypothermic after 2 hours (Slotman et al, 1985). In addition hypothermic patients reportedly spend up to one hour longer in the recovery ward resulting in further perioperative expenses (Conahan, 1982).

These general surgical causes of heat loss may be minimised by the adaptation of the temperature of the theatre environment, especially in children, and by protection against cutaneous heat losses by the use of metallic blankets and heat conserving devices. Warm irrigation fluids and infusion would also help to minimise heat loss and maintain core body temperature.

2.4.2. FACTORS RELATED TO INSUFFLATION

It has been previously assumed that laparoscopic procedures would have the benefit of helping to minimise the heat losses seen in the corresponding open operations, mainly due to the reduction of the surface area exposed for heat exchange by keeping the abdomen largely sealed. However despite this, it has been demonstrated that thermal losses occur during open and laparoscopic cholecystectomy (Wallasvaara, 1992). Previous studies have found that prolonged laparoscopic surgery time as compared to their open counterparts, CO_2 flow rates of greater than 3 litres/min to maintain pneumoperitoneum- and frequent gas extraction, for example to evacuate electrocautery smoke and air-leaks from ports, may partially account for the thermal losses seen in laparoscopic procedures (Ott, 1991 a; Seitzinger and Dudgeon, 1993).

Insufflators with built-in heating elements have been provided by some companies in an attempt to counteract the cooling effect of CO_2 gas insufflation, despite the lack of controlled evidence that such warming devices offer any hypothermia prophylaxis. It has now been shown, that devices currently available for the warming of insufflated gas confer no protection against laparoscopy-induced hypothermia (Bessell et al, 1995). This was an important discovery, because until this became clear many surgeons in the community had assumed the warm gas from their insufflators would be protecting their patients from hypothermia (perhaps forsaking

other precautionary measures), when in fact such assumptions have no physiological basis.

Thermodynamic calculations undertaken at the University of Adelaide Department of Mathematical Physics have indicated that humidification of the insufflated CO_2 should largely resolve the problem of laparoscopy-induced hypothermia.

2.5. POTENTIAL BENEFITS OF HUMIDIFIED GAS INSUFFLATION

2.5.1. IN LAPAROSCOPY

Therapeutic laparoscopy has been rapidly accepted world-wide and currently accounts for an increasing proportion of intra-abdominal procedures, yet the influence of laparoscopic surgery on temperature physiology has attracted little attention. Until recently it had been assumed that laparoscopy would virtually abolish the procedural loss of body heat compared to the corresponding "open" procedure, because with a "sealed" abdomen there should be less potential for heat loss from exposed surfaces. Yet the abdomen is not sealed off from the environment during laparoscopy. Indeed, gas flow rates passing over peritoneal surfaces during insufflation may exceed those during open laparotomy. This is supported by a recent randomised controlled animal study that determined that insufflation of CO_2 gas during laparoscopy resulted in a significant fall in core body temperature (Bessell et al, 1995). Because of the large numbers of patients undergoing laparoscopy, the uncorrected physiological insult of hypothermia, particularly during prolonged surgery, is considered to be a substantial problem.

To counteract the cooling effect of CO_2, insufflators with built-in heating elements

have become commercially available. However such devices currently available for the warming of insufflated gas confer no protection against laparoscopy-induced hypothermia (Bessell et al, 1995). This is because considerably more heat expenditure from the patient is required to evaporate body water to humidify the initially dry CO_2 stream, than is used to raise the ambient temperature of the CO_2 gas to body temperature. Humidified gas insufflation may contribute to the protection against laparoscopy-induced hypothermia.

Other studies report reduced postoperative pain following laparoscopy using insufflation gas at physiological temperature (Korell et al, 1996; Pier et al, 1994). It is hypothesised that under these circumstances the humidified gas insufflation may also result in postoperative pain reduction in comparison to standard dry gas insufflation due to a reduced physical trauma to the exposed membranes.

2.5.2. IN CLINICAL THORACOSCOPY

It is logical to assume that the potentially beneficial effects of humidified gas insufflation apply also to thoracoscopy since in many centres insufflation of CO_2 is used to hasten lung collapse on the side of the procedure when a double lumen endotracheal tube is used (Coltharp et al, 1992; Giudicelli et al, 1994; Landreneau et

al, 1992; Lewis et al, 1995), or alternatively to achieve lung collapse when a single lumen endotracheal tube is employed (Lewis et al, 1995).

It is hypothesised that humidification of insufflated gas during long thoracoscopic procedures might reduce postoperative hypothermia. It is also believed that the use of humidified gas might, by eliminating the desiccant effect of dry gas, reduce postoperative pain and thereby lower the incidence of postoperative sputum retention, atelectasis and pneumonia. Since postoperative pain is difficult to quantify in an animal model, this possible outcome can be assessed indirectly by examination of the morphologic effects on the parietal pleura of humidified gas insufflation, dry gas insufflation and no gas insufflation as a control.

2.5.3. IN PAEDIATRIC LAPAROSCOPY

Humidification of the gases insufflated in laparoscopic paediatric surgery has not been undertaken to date (Bissonnette et al, 1989 a and b; Bissonnette and Sessler, 1990; Bissonnette, 1992; Pintus et al, 1995; Rayman et al, 1995; Valla et al, 1991).

The problem is even more significant in children who, largely due to their greater body mass index (Figure 6), are particularly susceptible to hypothermia. This has been previously described in the perioperative context, as well as in the setting of

drownings and intoxications (Biggart and Bohn, 1990; Fretschner et al, 1993; Lamminpaa, 1994; Lamminpaa, 1995; Murat, 1994).

Perioperative temperature reductions - under the same perioperative conditions, especially with respect to standardised heat preservation (Belani et al, 1993; Bickler and Sessler, 1990; Morris, 1971; Morris and Kumar, 1972; Shanks et al, 1988; Sessler et al, 1992; Sessler, 1993; Stevens et al, 1971) - are predicted to be greater during longer paediatric procedures such as laparoscopic Nissen fundoplication. It is therefore suggested that children especially benefit from any core temperature saving effects produced by the use of humidified gas insufflation in laparoscopic surgery.

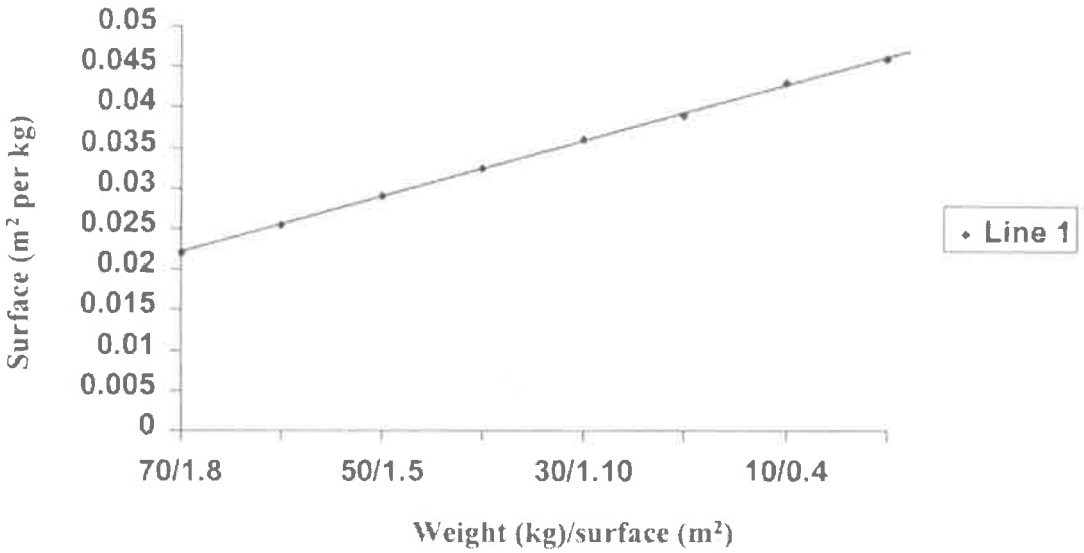

Figure 6 Body-mass-index: surface (m^2) per kg weight in relation to body weight (kg)

SECTION 3 METHODS

3.1. PORCINE LAPAROSCOPY

3.1.1. AIMS

It is hypothesised that humidification of insufflated CO_2 should largely resolve the problem of laparoscopy-induced hypothermia. The aim of this study was to confirm the contribution of water evaporation to heat loss, and evaluate the efficacy of insufflation with heated humidified gas in its prevention.

3.1.2. MATERIAL AND METHODS

The animal ethics committees of The Queen Elizabeth Hospital and the University of Adelaide granted ethical approval for this project. Five domestic white pigs weighing a median of 30 kg (range 24.5 - 49 kg) each received three different treatments on three separate occasions. The three treatments involved insufflating the animal with standard cool dry bottled gas on one occasion (21°C, 2% relative humidity (RH)), insufflating heated humidified gas on another occasion (40°C, 98% RH), and on an additional occasion, as a control procedure, no insufflation was performed. The order of these treatments was randomised and performed one week apart to allow the animal to recover from the anaesthetic.

In all animals the treatments were administered over 3 hours. Oesophageal temperatures were the primary outcome parameters measured at fifteen minute intervals by thermoresistors (series 700, Yellow Springs Instrument Co, Yellow Springs, Ohio, USA) displayed on a Tele-Thermometer (model 46, Yellow Springs Instrument Co, Yellow Springs, Ohio, USA). The ambient temperature of the theatre environment was also recorded and maintained close to 24°C.

All treatments were conducted under aseptic conditions in a dedicated operating theatre with the animals anaesthetised during all procedures. The animals received a single perioperative dose of intramuscular penicillin (Penicillin G, Commonwealth Serum Laboratories, Melbourne, Australia), were sedated using intramuscular ketamine (Ketalar, Parke-Davis, Australia), and anaesthetised with intravenous pentobarbitone sodium (Nembutal, Boehringer Ingelheim, Germany) prior to endotracheal intubation. Anaesthesia was maintained by ventilation of a 1.0 - 1.5% halothane/O_2 mixture (Fluothane, ICI Drugs, Australia), through a closed anaesthetic circuit with a spirometer and heat and moisture exchanger included in the anaesthetic circuit. A metallic reflective blanket was wrapped around the animal to reduce thermal loss from cutaneous exposure. After the final treatment each animal was killed by a lethal intravenous dose of pentobarbitone before reversal of anaesthesia.

Control animals received no insufflated gas, but animals in the two experimental groups received CO_2 gas delivered through a LINS-1000 insufflator (Cook Medical Technology, Queensland, Australia) (Figure 7) connected to a 10 mm port (Ethicon, Australia) inserted into the peritoneal cavity through the umbilicus. Before entering

the port the gas flowed through a chamber containing a temperature and humidity probe (HMP 35, Vaisala Pty Ltd, Helsinki, Finland, ± 1.0% RH) (Figure 8) connected to an indicator unit (HMI 31, Vaisala Pty Ltd) which monitored the temperature and humidity of gas entering the animal throughout the experiment. In the group receiving heated humidified gas, a heating and humidification chamber (Fisher and Paykel, Australia) (Figure 9) was placed in series upstream from the temperature and humidity probe. Approximately 15 minutes was allowed for the gas to heat and humidify to the requisite level before the commencement of insufflation. The consistency of the temperature and humidity output using this apparatus had previously been confirmed during in vitro experiments. The afferent gas line also incorporated an insulated heating coil that maintained the humidified CO_2 at a temperature of 39°C. The abdominal pressure was maintained at 10 mmHg. A second 10 mm port was positioned supra-umbilically and a standardised CO_2 leak of 10 litres/min was established by fully opening the three-way stopcock, and confirmed by insufflator flow rates. This was performed to simulate the repeated gas losses that are experienced clinically during some advanced laparoscopic operations. Another chamber also containing a temperature and humidity probe was connected to the exsufflated CO_2 line to measure temperature and humidity as it exited the abdominal cavity (Figure 10). The temperature and humidity of insufflated and exsufflated gases were recorded at 15 minute intervals over the 3 hour period as secondary outcome parameters.

3.1.3. INSTRUMENTS

3.1.3.1. Modified LINS-1000 insufflator

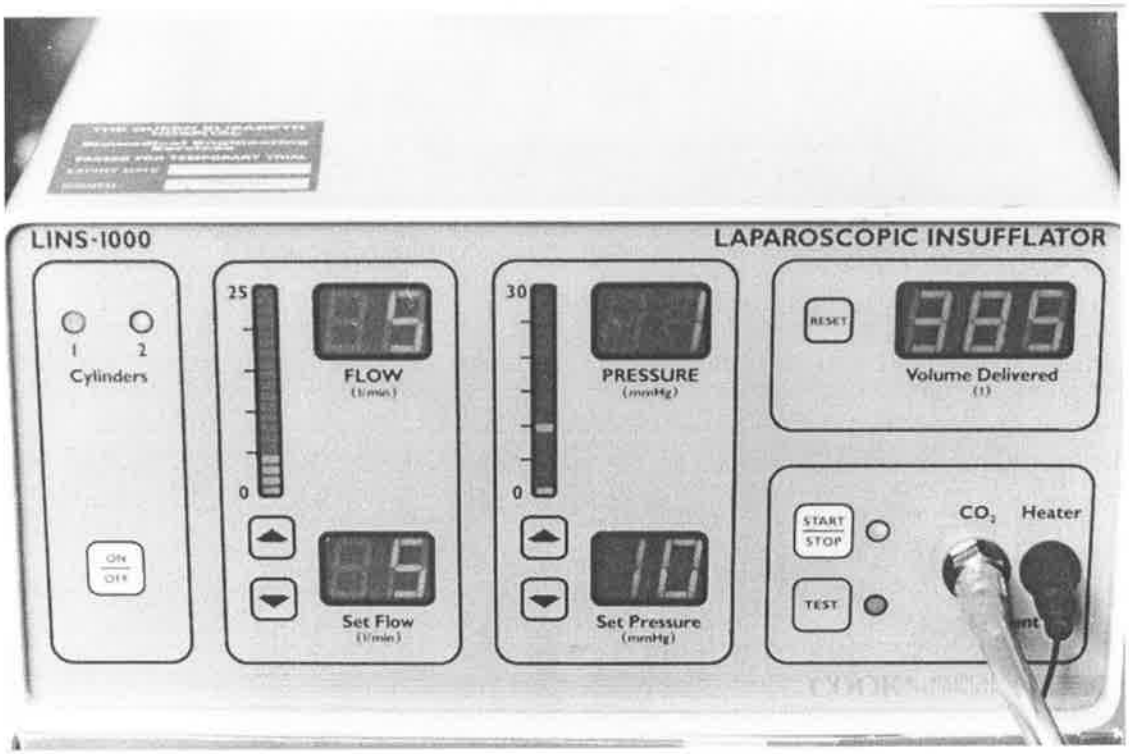

Figure 7 LINS- 1000 - insufflator

3.1.3.2. Temperature and humidity probe

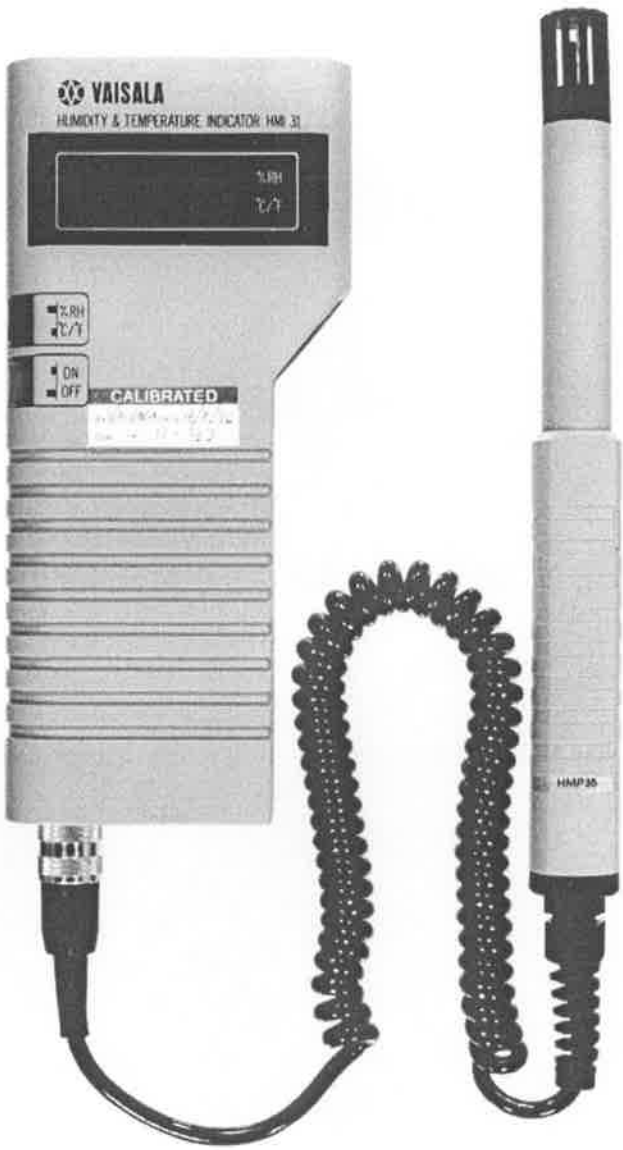

Figure 8 Temperature and humidity probe

3.1.3.3. Humidification chamber

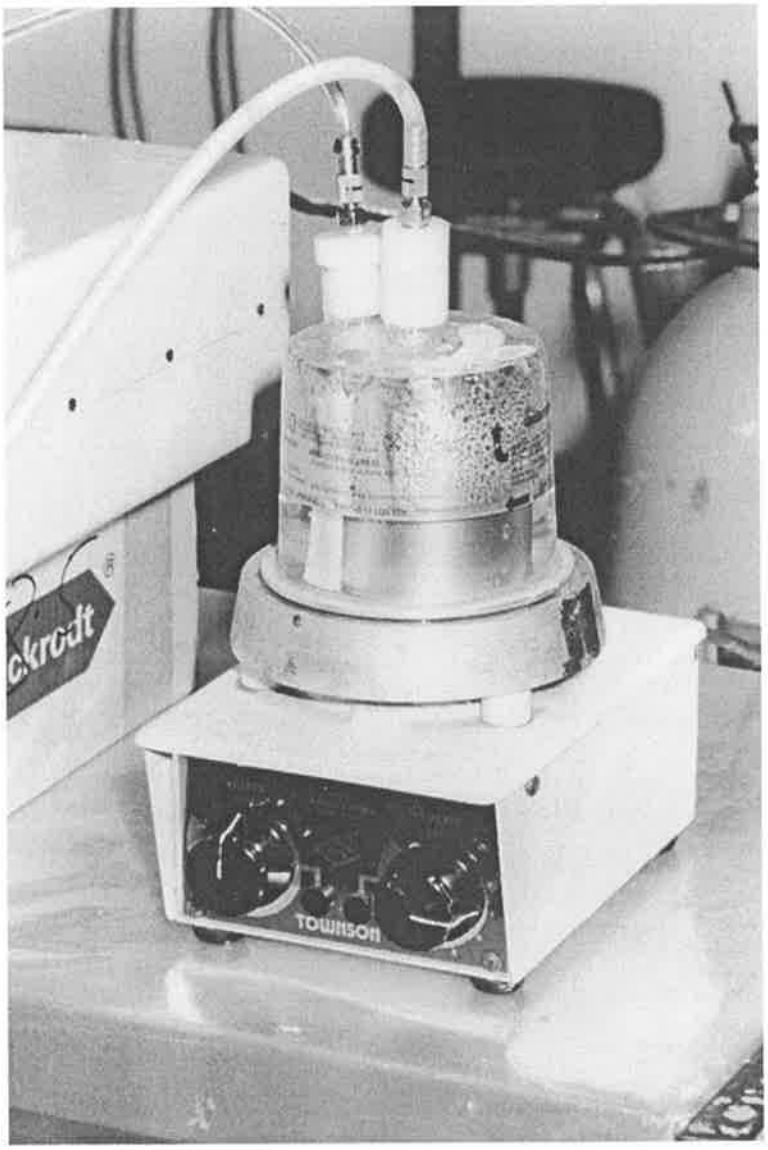

Figure 9 Heating and humidification chamber

3.1.3.4. Probe chamber

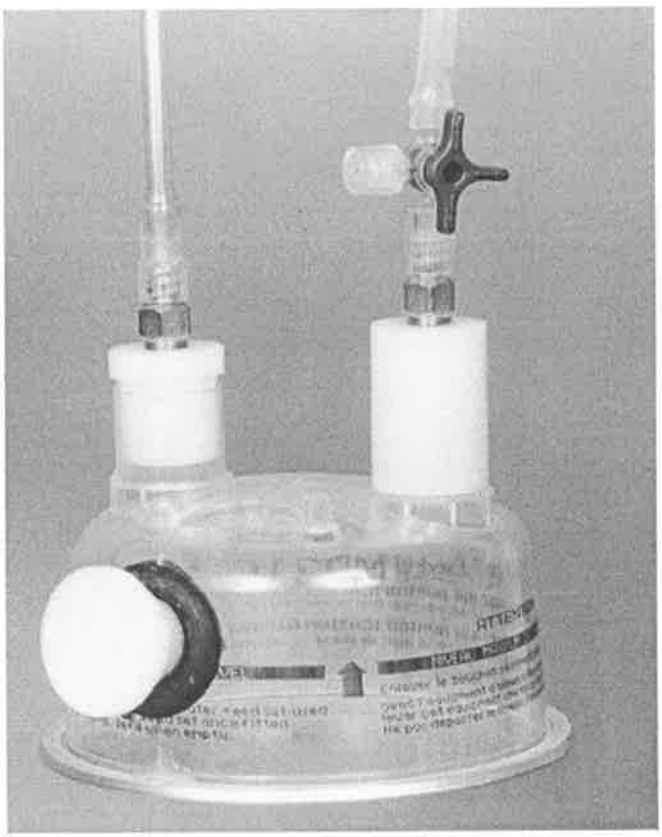

Figure 10 Probe chamber

3.1.4 THERMODYNAMICS

South Australian Domestic White Pig , mass = m = 30 kg
Insufflation flow rate (cool,dry gas) of 10 litres(L)/min for 3 hours
Effluent gas is being measured for temperature and humidity
The animal's body temperature is being continually measured

How much of the temperature drop is due to water evaporation ?

Water content of the insufflating gas:

Temperature	=	24°C	
Humidity	=	5.2%	
Absolute humidity at 24°C	=	22mg/L	
Gas volume over 3 hours	=	1800L	
Ingoing water	=	1800 x 22 x 5.2/100 =	2059mg water

Water content exiting the pig:

Temperature	=	29.52°C	(averaged over 3 hours)
Humidity	=	95.97%	(averaged over 3 hours)
Absolute humidity at 29°C	=	28mg/L	
Gas volume over 3 hours	=	1800L	
Outgoing water	=	1800 x 28 x 95.97/100 =	48368.88mg water

Water evaporated (over the 3 hours)	=	46309.88mg water

Latent heat of vaporisation of water at the pig temperature

= 2.43 MJ/kg
= 2.43 J/mg

Heat expended evaporating the water = 112533J

Specific heat capacity of pig tissue
= 3.5kJ/kg

Absolute heat capacity of this pig
= 30 x 3.5 = 192.5kJ = 192500J

Temperature fall of pig due to evaporation of water

= 192500/112533 = **1.71ºC**

1. Heat required to raise temperature of CO_2 gas from 25°C to 37°C.

Heat	=	Q	=	m s (t2-t1)		
Specific heat	=	s	=	constant at constant pressure		
Specific heat of CO_2			=	∂R		
			=	1.30 x 8.31 J/mole/K		
mass	=	m	=	10 litres/min	=	6.8×10^{-3} mol/s at 25°C

Q = s m (t2-t1)

= $(6.8 \times 10^{-3}$ mol/s) x (1.30 x 8.31 J/mol K) x 12°

= **0.9 Watts (or J/S)**

2. Heat required to evaporate water in the pig to saturate the initially dry CO_2 stream of 10 L/min measured at 25^0C

Daltons Law:

Heat = Q = mL

Latent heat = L = 43×10^3 J/mol at 37^o

p V = n R T

p H_20 at 37^oC = 47 mm of Hg
= 47 x 133 pascals

Number of moles H_20 evaporated

$$n(m) = \frac{p\ V}{R\ T} = \frac{(47 \times 133\ Pa) \times 10/60 \times 10^{-3}\ m\ 3/5)}{(8.31\ J/mol\ K) \times (298K)}$$

$$= 4.2 \times 10^{-4}\ mol/s$$

Heat required:

$$Q = m\ L = (4.2 \times 10^{-4}\ mol/s)\ (43 \times 10^3\ J/mol)$$

$$= \underline{\mathbf{18\ Watts}}$$

The evaporation of body water to saturate the CO_2 is a much greater source of heat utilisation.

3. Temperature Drop after 3 hours:

Q	=	m s (t2-t1)		
s	=	specific heat water at 37°	=	4180 J/kg K
m	=	mass of pig	=	30 kg
Q	=	18 Watts x (180 min x 60s) J		

$$t2 - t1 = \frac{Q}{s\ m}$$

$$= \frac{18 \times 180 \times 60}{30 \times 4180} = \underline{\mathbf{1.6^{o}C}}$$

Conclusion: Within the errors of measurement, this accounts for most of the observed temperature drop of 2°.

Note: Warming the CO_2 would be ineffective, however pre-saturating it with water vapour (by passing through a bubbler) should solve the problem.

3.1.5. STATISTICAL ANALYSIS

To analyse changes in the primary outcome parameter of oesophageal and intraperitoneal temperature, repeated measures analysis of variance was used, with grouping factors of treatment (no gas, cool dry gas, heated humidified gas) and a within factor of time. This method of analysis was the most appropriate for the described experimental situation. Analysis was performed using 5V, BMDP statistical software UCLA (1991), and a difference was regarded as significant at an alpha level of 0.01. The secondary outcome parameter of temperature and relative humidity of insufflated and exsufflated gas, were statistically summarised as means accompanied by 95% confidence intervals, as changes over time were not considered.

3.2. LAPAROSCOPIC CHOLE-CYSTECTOMY

3.2.1. AIMS

Recent animal trials have reported that core body temperature falls during laparoscopy, and is dependent on the duration of insufflation rather than the temperature of the insufflated gas (see chapter 4.2.). This hypothermic effect of laparoscopic insufflation is absolved by the use of humidified gas (Bessell and Maddern, 1998). Other studies report reduced postoperative pain following laparoscopy using insufflation gas at physiological temperature (Korell et al, 1996).

The aim of this pilot study was to determine the beneficial effects, if any, of insufflation of humidified carbon dioxide (CO_2) gas during laparoscopic surgery in the clinical setting. Specifically, it was hypothesised that humidified gas insufflation resulted in greater heat preservation and postoperative pain reduction in comparison to standard dry gas insufflation.

3.2.2. MATERIAL AND METHODS

The study was approved by the Human Ethics Committee of The Queen Elizabeth Hospital. After preoperative written consent, forty consecutive unselected patients underwent laparoscopic cholecystectomy during a period of four months. Twenty patients were randomised to receive humidified CO_2, and twenty control patients were randomised to receive standard CO_2 insufflation to create the pneumoperitoneum.

Before entering the umbilical port, insufflated gas flowed from a modified LINS-1000 insufflator. In the group receiving humidified gas, the insufflator tubing (Figures 11, 13) (Cook Medical Technology, Queensland, Australia) incorporated a humidification chamber (Figures 14-16) to generate relative humidity of 88 to 90%. The afferent gas line also incorportated an insulated heating coil (Figure 12) which maintained the humidified CO_2 at a temperature of 34.0 to 37.0°C. The consistency of the temperature and humidity output using this apparatus had previously been confirmed during in vitro experiments. In the group receiving standard dry insufflation gas no such humidification chamber or insulated heating coil were incorporated in the afferent insufflator tubing, thereby delivering gas at a temperature of 21.2 to 25.2^0 C and relative humidity 0.0 to 5.0 % to the patient.

The operation was performed using a standardised four port technique by seven different surgeons. Standardised routine general anaesthesia was administered by

eleven different anaesthetists. No premedication was given, and the only intraoperative analgesics used were fentanyl (Astra, New South Wales, Australia) and morphine sulfate (David Bull Laboratories, Victoria, Australia). The inhalational anaesthetic used was forthane (Abbott, South Australia, Australia) mixed with oxygen. The ambient temperature of the theatre environment was recorded with a mean room temperature of 21.1° C in both groups.

The two main outcome measures were core body temperature and postoperative pain. Body temperature was recorded by means of an oesophageal thermoresistor (Vital-Temp™ Vital Signs Inc, New Jersey, USA) every fifteen minutes. Postoperative analgesia was administered by ward nursing staff and recorded in the bedside drug chart from a standardised prescription of intramuscular morphine sulphate (David Bull Laboratories, Victoria, Australia) 10 mg four hourly, or oral or rectal Paracetamol (Fawns & McAllan Pty Ltd, Victoria, Australia) 500 mg six hourly. All patients were personally reviewed 6 hours after completion of the operation, and again on days 1, 2 , 3 and 4 if they remained inpatients. Patients were contacted on day 10 by telephone or personally in the outpatient clinic. On each occasion the patients were questioned regarding their pain levels, which were pointed out by the patient on a visual analogue pain score device ranging from 0 to 10. In addition, the patients were asked when they had returned to normal activity and to work, and of any complications.

For both operations intraoperative records were kept of core body temperature, electrocardiographic abnormalities, CO_2 volume consumed during the operation, and endoscopic visibility. Postoperative INR and platelets counts were also recorded.

3.2.3. INSTRUMENTS

3.2.3.1. Humidifying insufflation tubing

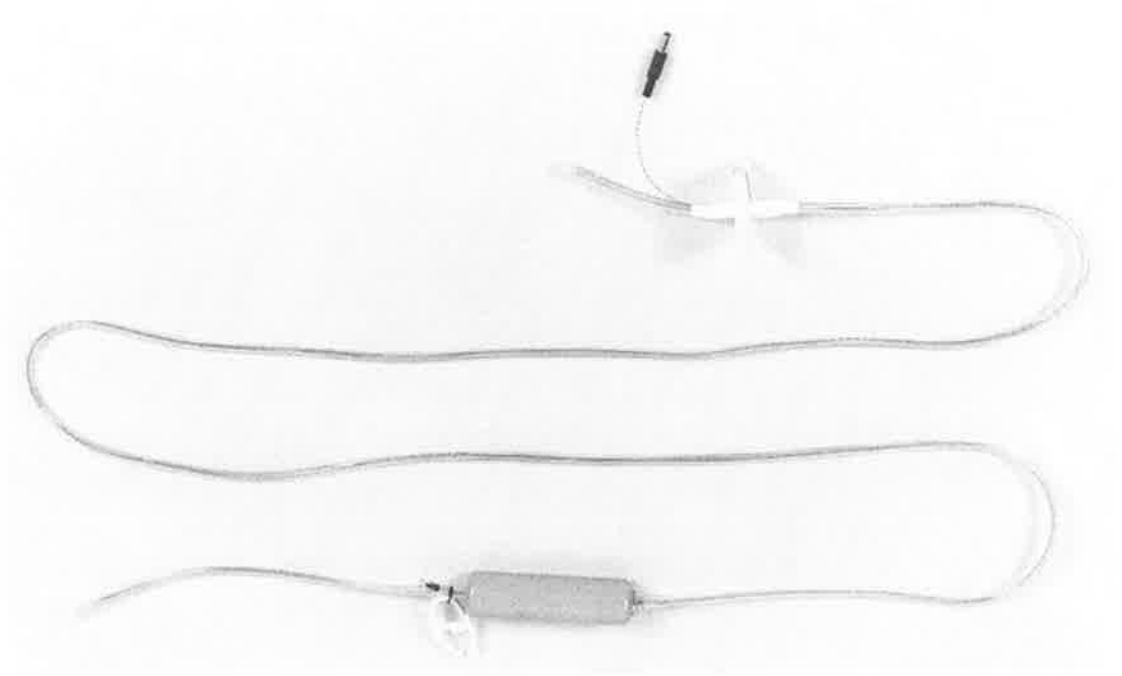

Figure 11 Humidifying insufflation tubing
(top end : connection to insufflator (Figure 7)

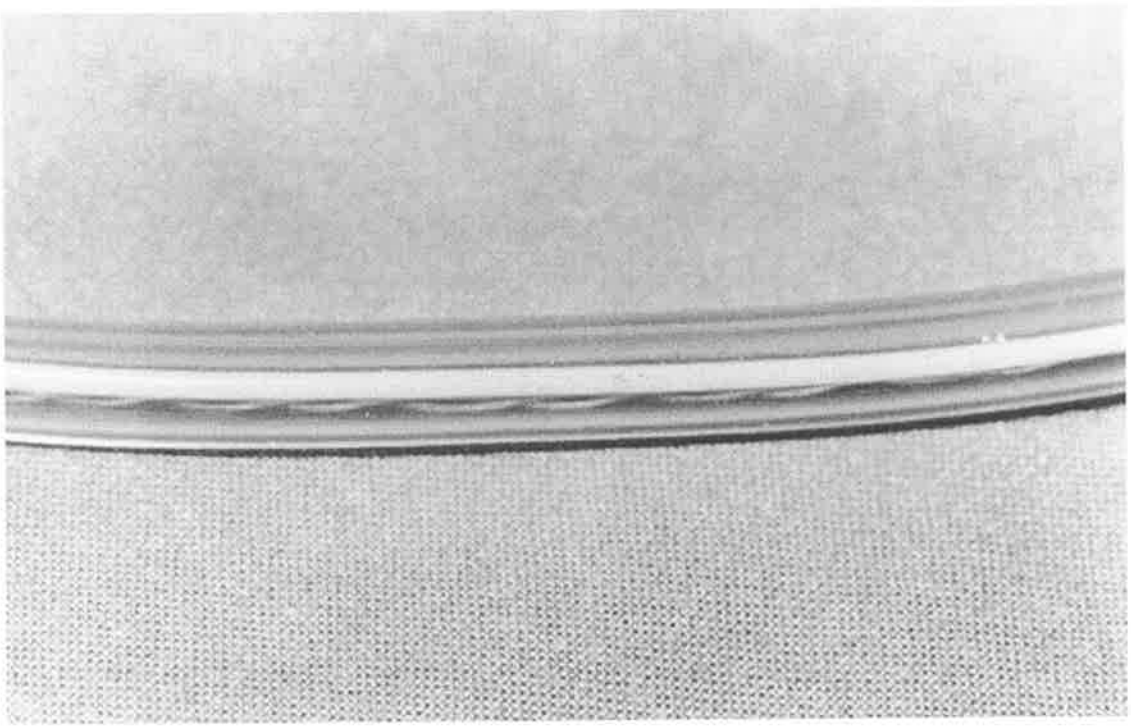

Figure 12 Humidifying insufflation tubing : heating coil

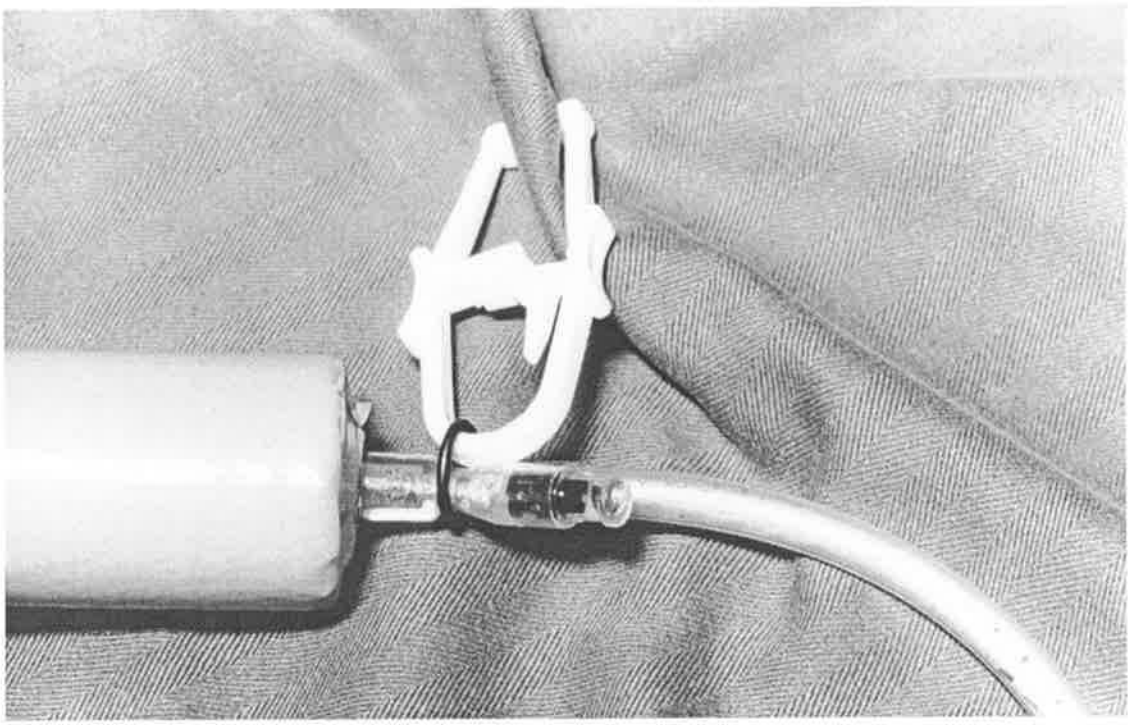

Figure 13 Humidifying insufflation tubing : humidification chamber with water injection site

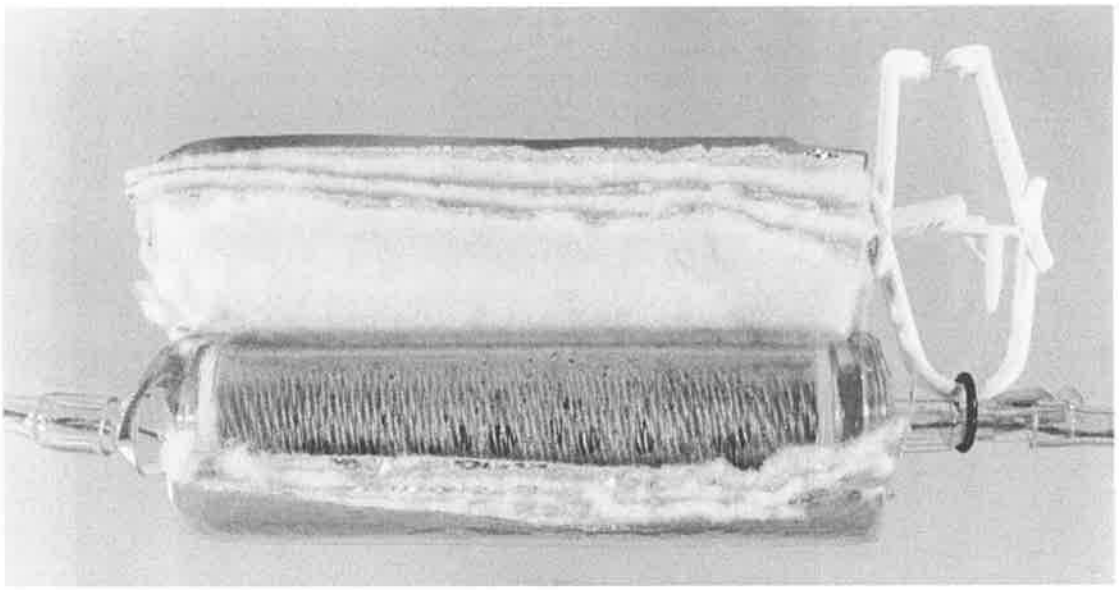

Figure 14 Humidification chamber, insulation opened

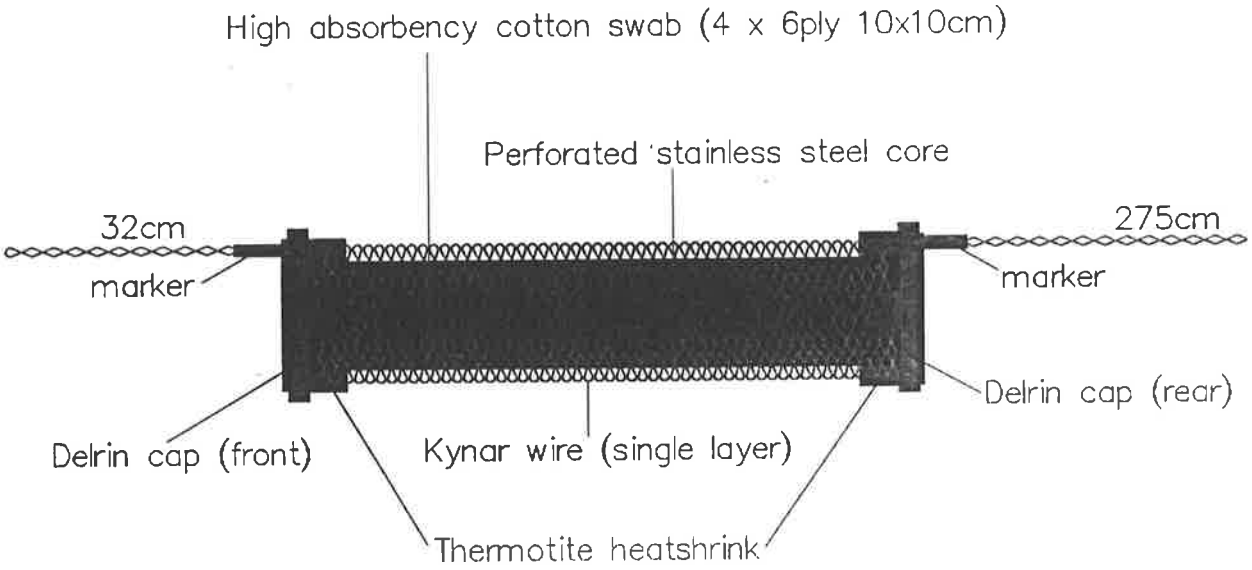

Figure 15 Humidification core

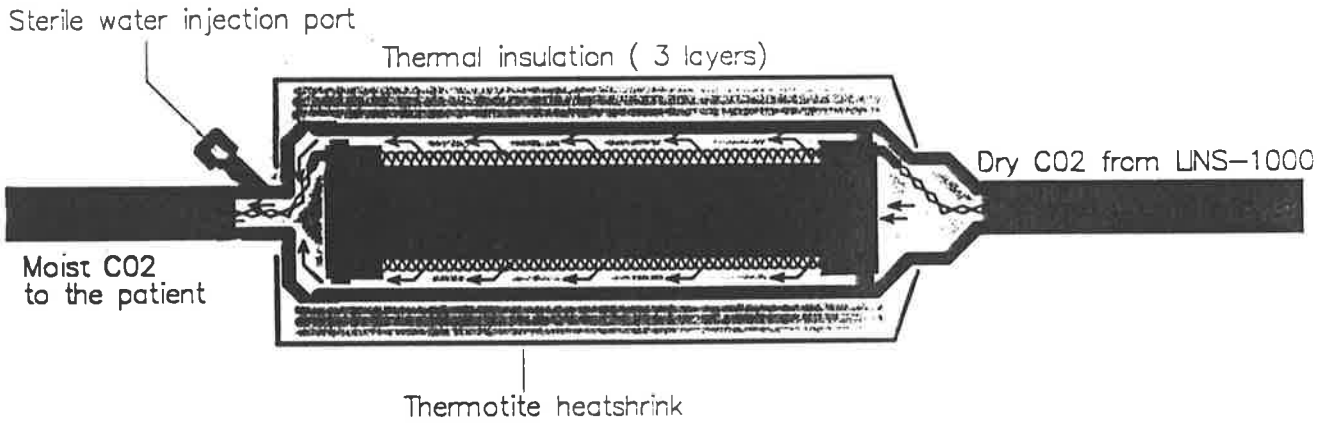

Figure 16 Humidification chamber

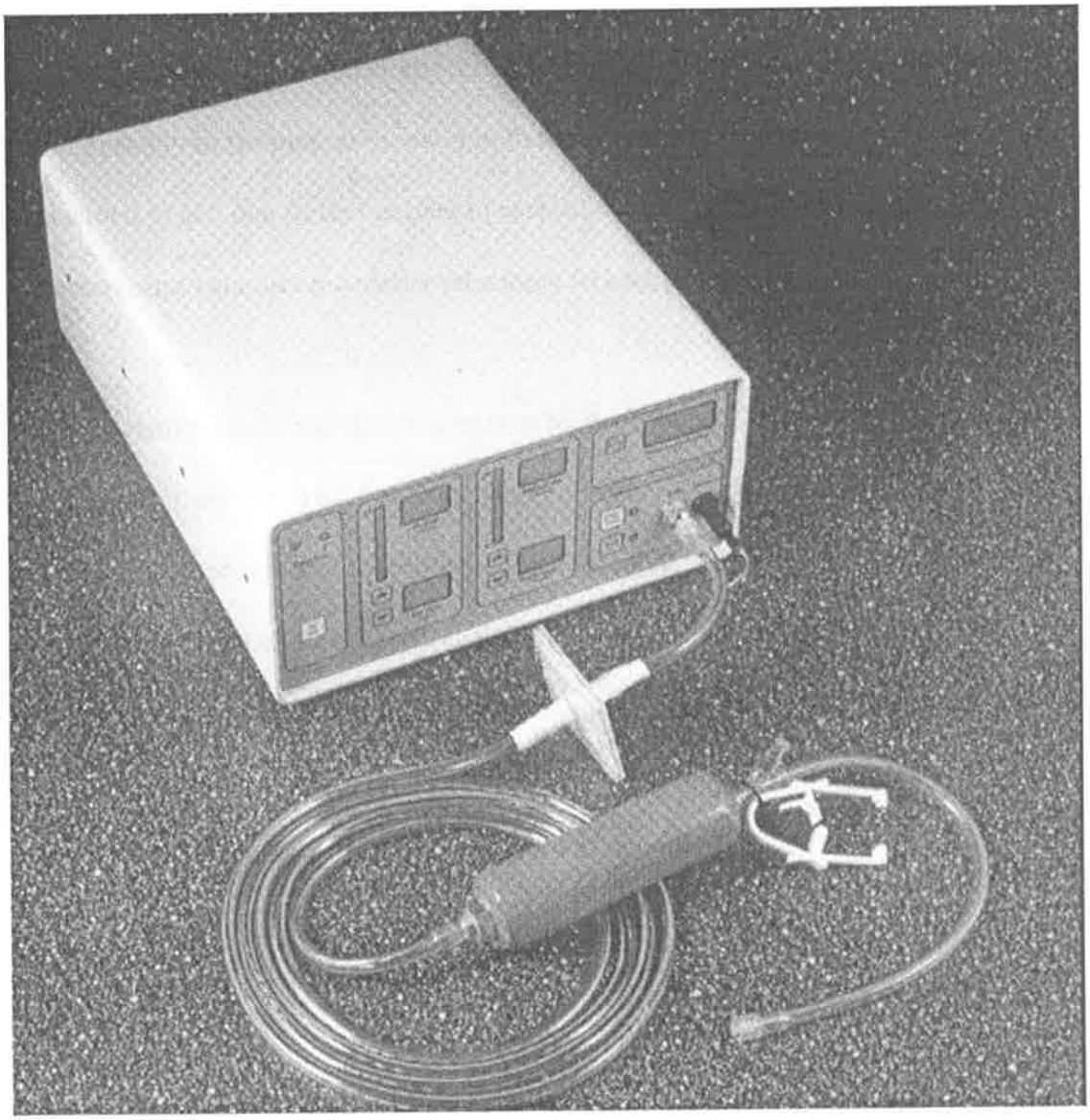

Figure 17 Humidifying insufflation tubing connected to insufflator

3.3. PORCINE THORACOSCOPY

3.3.1. AIMS

Evidence suggests that beneficial effects may be derived from the use of humidified gas for insufflation during minimally-invasive surgery. A study in pigs found that postoperative hypothermia could be avoided by the use of humidified insufflation gas during laparoscopy (see chapter 4.1.), while a recently completed clinical trial in the Department of Surgery, The Queen Elizabeth Hospital investigating humidification of insufflated carbon dioxide (CO_2) during laparoscopic cholecystectomy has shown a significant reduction of postoperative pain in those patients receiving humidified gas (see chapter 4.2.).

The objective of the present study was to determine if such beneficial effects of humidified gas insufflation apply also to thoracoscopy as in many centres insufflation of CO_2 is used to hasten lung collapse on the side of the procedure when a double lumen endotracheal tube is used (Coltharp et al, 1992; Giudicelli et al, 1994; Landreneau et al, 1992; Lewis et al, 1995), or alternatively to achieve lung collapse when a single lumen endotracheal tube is employed (Lewis et al, 1995).

It was hypothesised that humidification of insufflated gas during long thoracoscopic procedures might reduce postoperative hypothermia. It was also hypothesised that the use of humidified gas might, by eliminating the desiccant effect of dry gas,

reduce postoperative pain and thereby lower the incidence of postoperative sputum retention, atelectasis and pneumonia. Since postoperative pain is difficult to quantify in an animal model, this possible outcome was assessed indirectly by examination of the morphologic effects on the parietal pleura of humidified gas insufflation, dry gas insufflation and no gas insufflation as a control.

3.3.2. MATERIAL AND METHODS

Six specific pathogen-free Domestic White Pigs (Pig and Poultry Production Institute, Roseworthy, South Australia) weighing initially between 31 kg and 34 kg were utilised. Three separate studies performed on each animal looked at the effects on body temperature and pleural histopathology of first, insufflation of warmed, humidified CO_2, second, insufflation of dry gas and third, the insertion of the usual thoracoscopy ports but no gas insufflation. The three studies were each of three hours duration; they were performed in random order and one week apart to allow for recovery of the animal between studies.

The studies were performed under general anaesthesia. Sedation was achieved with subcutaneous azaperone (Stresnil, Janssen Pharmaceutica, Australia) or ketamine (Ketalar, Parke-Davis, Australia) and anaesthesia was induced with inhalation of halothane (Fluothane, ICI Drugs, Australia) in oxygen. Following placement of either a left-sided double-lumen endobronchial tube (28 Fr.) or a 7.5 mm

endotracheal tube (Mallinckrodt Medical Inc, St. Louis, USA), anaesthesia was maintained with 1.0 - 1.5% halothane in oxygen with a fresh gas flow set for each animal and with intermittent positive pressure ventilation adjusted to maintain the end-tidal CO_2 close to 35 mm Hg. When using the single lumen endotracheal tube the lung on the side of thoracoscopy was seen to fall away from the chest wall when the thoracic cavity was opened. This tube was used in the last three animals in preference to the double-lumen endobronchial tube since animal No. 2 died during its second study and animal No. 3 died two hours into its first. At autopsy both pigs were found to have the left upper lobe originating from the trachea, thus making single lung ventilation of the left lung for long periods extremely hazardous and adequate oxygenation impossible. Oxygen saturation and partial pressure of end-tidal CO_2 were continuously monitored (Datex Oscar Multigas Monitor and Pulseoximeter, Datex Instrumentarium Corp, Helsinki, Finland). Electrocardiographs were obtained hourly (Nikon Kotiden Cardiofax, Kogyo Co Ltd, Japan).

After supine positioning, a metallic reflective blanket was wrapped around the animal to reduce thermal losses from cutaneous exposure. Two 10 mm thoracoscopic ports (Ethicon, Australia) were inserted via the right 4th and 5th intercostal spaces anterolaterally, and insufflating CO_2 set at a fresh gas flow of 5 litres per min was delivered to one of the ports from a modified LINS-1000 insufflator (Cook Medical Technology, Queensland, Australia) via a humidifying chambre (Fisher and Paykel, Australia) and a probe chamber (Fisher and Paykel, Australia) for measurement of the temperature and humidity at standardised length

tubing. Gas flow exiting to the atmosphere from the second thoracoscopy port passed via another probe chamber to allow measurement of the temperature and humidity of the exiting gases. The large diameter of the outflow tubing resulted in the pressure in the right thoracic cavity being close to ambient, with the elastic recoil of the lung resulting in its falling away from the chest wall. For the study using warmed, humidified insufflation gas, the gas flow was warmed to 38.6°C and actively humidified to between 86% and 99%, while for the study using dry gas the flow was passed through the same system but without heating and humidification and at a recorded temperature of 23.5°C.

Temperature and relative humidity of both the insufflated and the exiting gases were checked at 15 minute intervals using a temperature and humidity probe (HMP 31 and 35, Vaisala Pty Ltd, Helsinki, Finland). Pre-set room temperature was also recorded at 15 minute intervals and was maintained at 21.5°C during all procedures.

Core body temperature, one of the two main outcome parameters, was measured at 15 minute intervals by an oesophageal thermoresistor (Yellow Springs Instrument Co, Series 700, Yellow Springs, Ohio, USA) displayed on a Tele-Thermometer (Yellow Springs Instrument Co, Model 46 Yellow Springs, Ohio, USA).

The other main outcome parameter, the morphological changes in the parietal pleura, was determined after each three hour study period by excision-biopsy of a 5 x 5 mm

specimen of parietal pleura which was sent for light and electron microscopic examination by blinded examiners.

Approval for this project was granted by the Animal Ethics Committees of The Queen Elizabeth Hospital and the University of Adelaide. All procedures were performed under aseptic conditions, and each animal was anaesthetised for the duration of each study. Before reversal of anaesthesia all ports were removed and muscular, fascial and skin defects closed with sutures. As only two 10 mm ports were used, postoperative analgesia was not indicated. At the completion of the final studies, the animals were killed by an intravenous overdose of phenobarbitone (Membutal, Boehringer Ingelheim, Germany). Autopsies were performed on all animals.

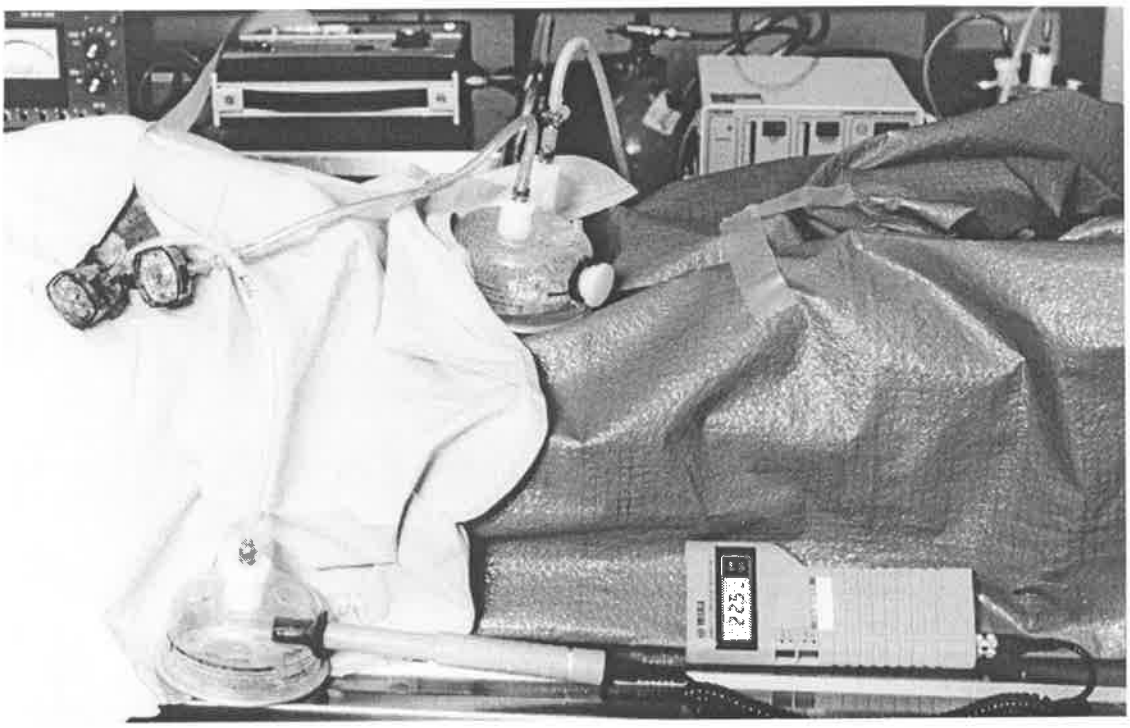

Figure 18 Experimental set-up for humidified gas insufflation: from left to right

Background: Thermoresistor, electrocardiogramm, insufflator, heating and humidification chamber
Middle: Thoracoscopic ports with tubing lines, probe chamber, metallic blanket
Foreground: Probe chamber, temperature and humidity probe

3.3.3. INTUBATION AND PRESENCE OF TRACHEAL UPPER LOBE BRONCHUS

3.3.3.1. Introduction

A double lumen tube was used to achieve lung separation in the first three animals studied. When the second and third pigs died unexpectedly in the course of the study and were found at autopsy to have a left main bronchus originating from the trachea (Figure 21), a decision was taken to conduct the remaining studies using a single lumen endotracheal tube. Autopsies revealed the normal porcine bronchial configuration in three of the six pigs, with the right upper lobe bronchus originating from the trachea (Nakakuki, 1994) (Figures 19 and 20). In the other three, which included the two that died unexpectedly, it was the left upper lobe bronchus which originated from the trachea. The configuration of the bronchial anatomy of all six animals is presented, and recommendations made for improved management procedures for single-lung ventilation in pigs.

3.3.3.2. Material and methods

All studies were performed under general anaesthesia which involved sedation with intramuscular ketamine (20 mg/kg) and xylazine (Tarnell Laboratories, Australia) (1.5 mg/kg), induction with halothane in oxygen via a face-mask and maintenance

with halothane in oxygen and with intermittent positive pressure ventilation adjusted to maintain the end-tidal carbon dioxide close to 35 mm Hg. The animal was positioned supine, oxygen saturation and the partial pressure of end-tidal carbon dioxide were continuously monitored (Datex Oscar Multigas Monitor and Pulseoximeter, Datex Instrumentarium Corp, Helsinki, Finland), with the pulse oximeter probe placed on the tip of the pig's tail, and electrocardiographs were obtained hourly (Nikon Kotiden Cardiofax, Kogyo Co Ltd, Japan).

In the first three animals a 28 Fr. left-sided double-lumen endobronchial tube (Mallinckrodt Medical Inc, St. Louis, USA) was used to achieve lung separation. With the tube held straight by a wire introducer placed in the bronchial lumen, the larynx was intubated under direct vision using a long straight-bladed laryngoscope. Once in the trachea and the introducer removed, the tube had to be advanced well beyond its full length so necessitating the use of 7.0 cm long extensions to both lumens of the double-lumen tube. Lung separation was achieved by inflating the bronchial cuff of the double-lumen tube, and optimal placement determined by hand-ventilating each lung in turn while monitoring not only inflation pressures but also the observed inspiratory and expiratory flow. Auscultation of the chest to determine the adequacy of upper lobe ventilation was found not to be helpful, probably due partly to the relatively narrow upper thorax in the pig and partly, in retrospect, to the fact that the physical configuration of the double lumen tube aligned very poorly with the pig's bronchial anatomy.

One-lung anaesthesia was uneventful in the first pig which was studied on three separate occasions, each of 3 hour duration. The first 3 hour study on the second pig was also uneventful. However, this animal arrested and died in the course of its second study. A post-mortem examination revealed a left main bronchus originating from the trachea.

The third pig also arrested and died, in spite of even closer monitoring of one-lung ventilation. The first warning that all was not well was, in retrospect, the manifestation, two hours into the study, of "poor signal" problems with the pulse oximeter probe. Probe 'pick up' was not improved by attempts to adjust the position of the probe on the tip of the animal's tail, and a sudden falling off in end-tidal carbon dioxide immediately preceded cardiac arrest. Two-lung ventilation was re-introduced and external cardiac massage was performed unsuccessfully. Since a paediatric fiberoptic bronchoscope was not available to ensure optimal double-lumen tube placement, the study protocol was modified for the remaining pigs to allow ventilation via a single-lumen endotracheal tube.

Autopsies revealed that in each of the six animals the upper lobe bronchus of either the left or the right lung originated directly from the trachea. In three pigs it was the right upper lobe bronchus, and in the other three the left upper lobe bronchus. Figure 22 shows the dissected tracheobronchial tree of the third pig photographed adjacent to the left-sided double lumen tube which was used. The main bronchi were very short in all animals and where the upper lobe bronchus arose from the trachea, there was an almost non-existent 'main bronchus' to the rest of that lung.

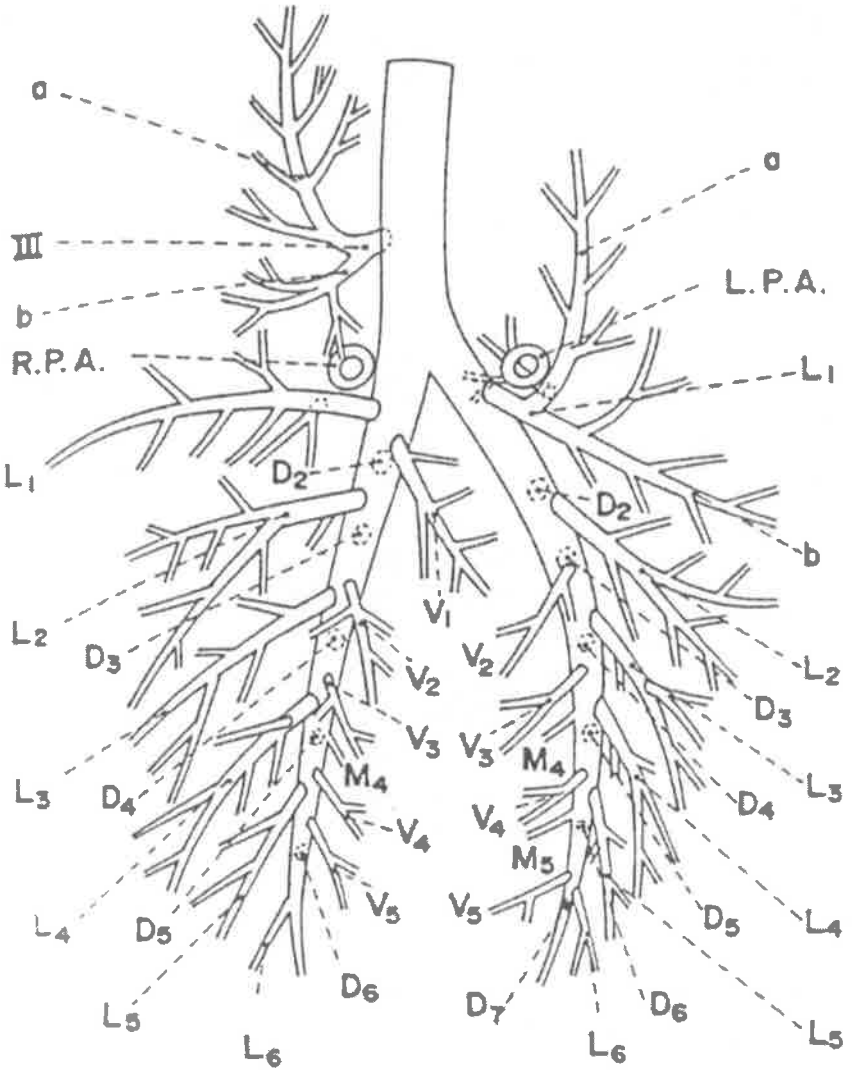

Figure 19 Tracheobronchial tree of suis species

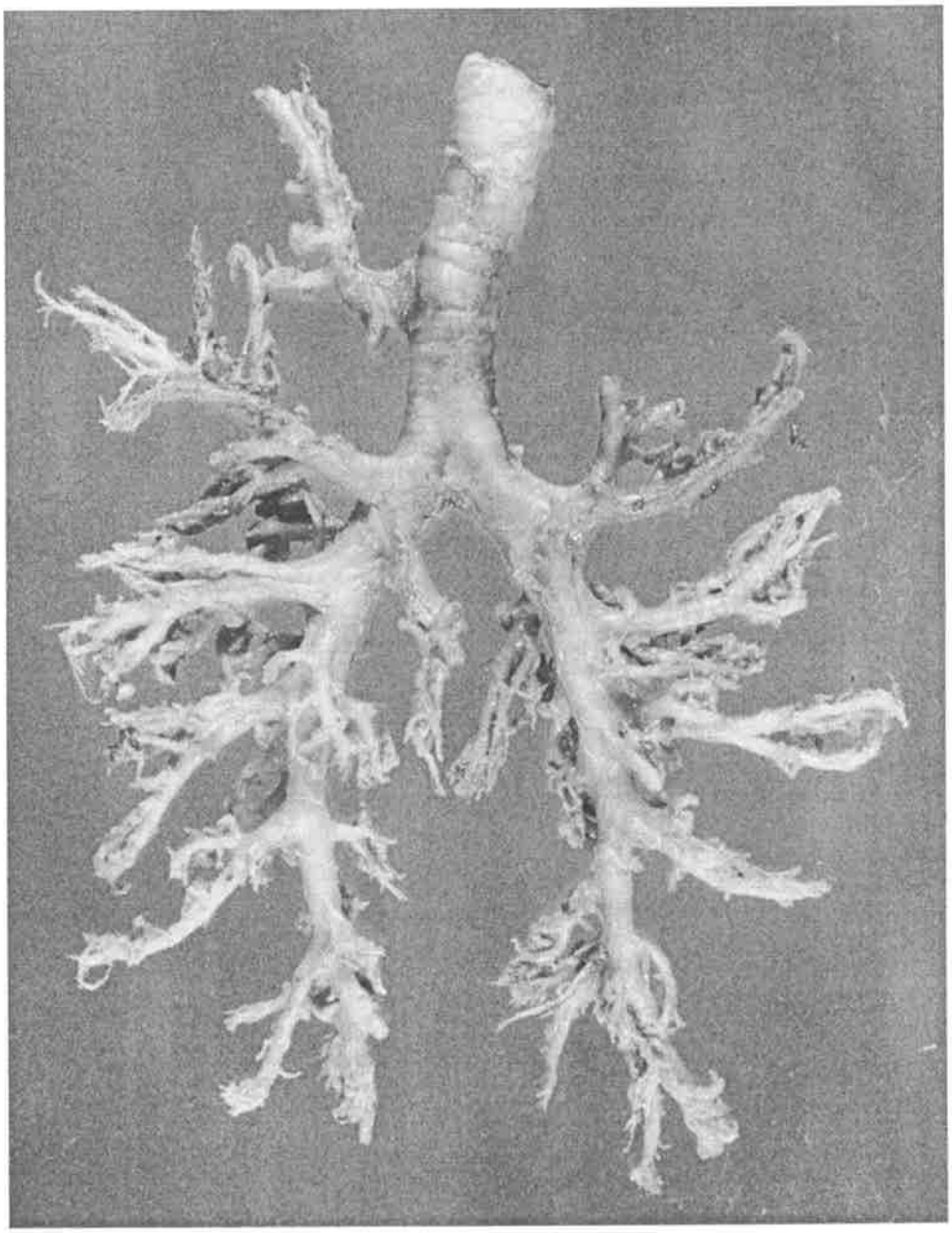

Figure 20 Tracheobronchial tree of South Australian Domestic White Pig with right tracheal upper lobe bronchus

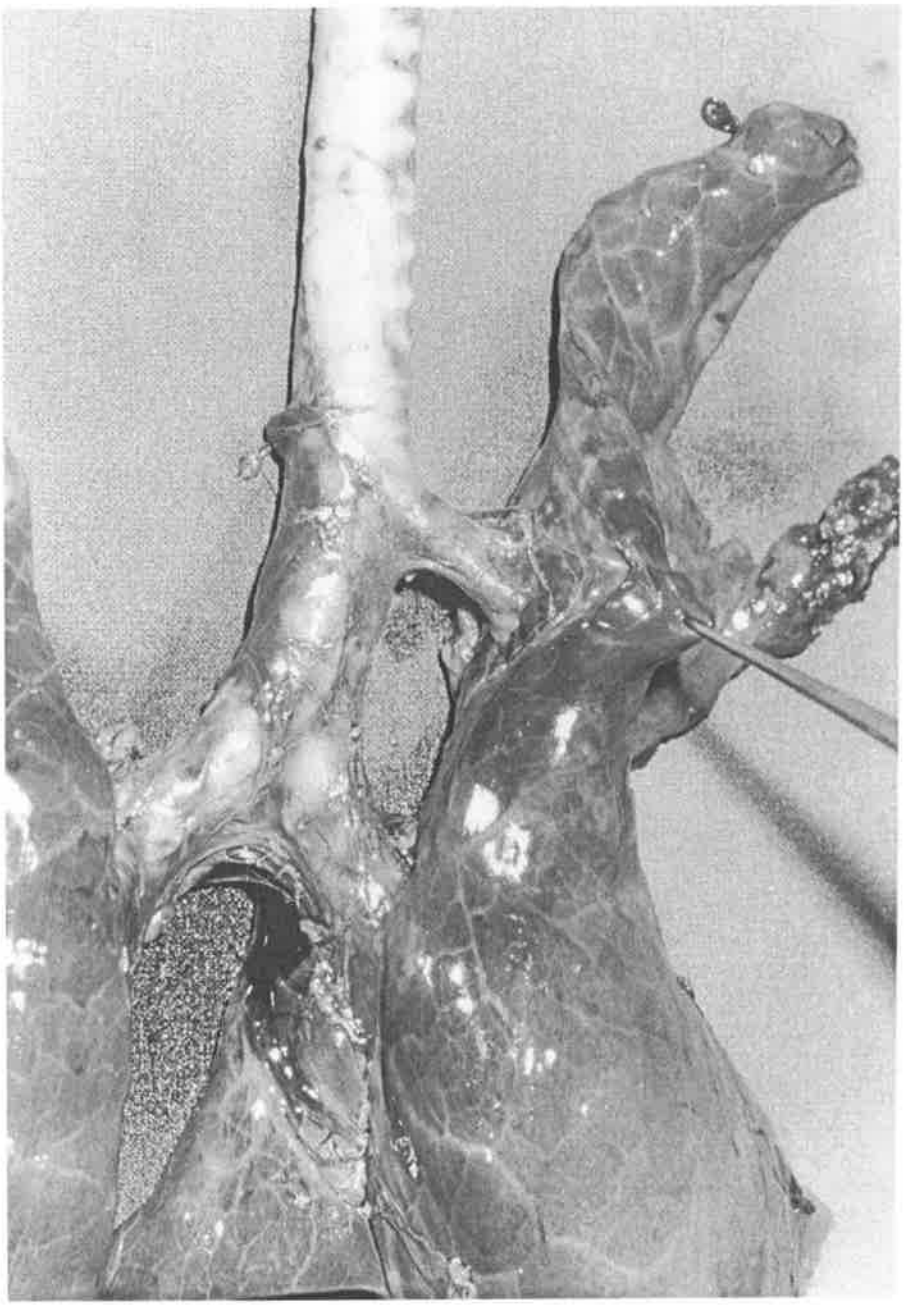

Figure 21 Left tracheal upper lobe bronchus.

South Australian Domestic White Pig

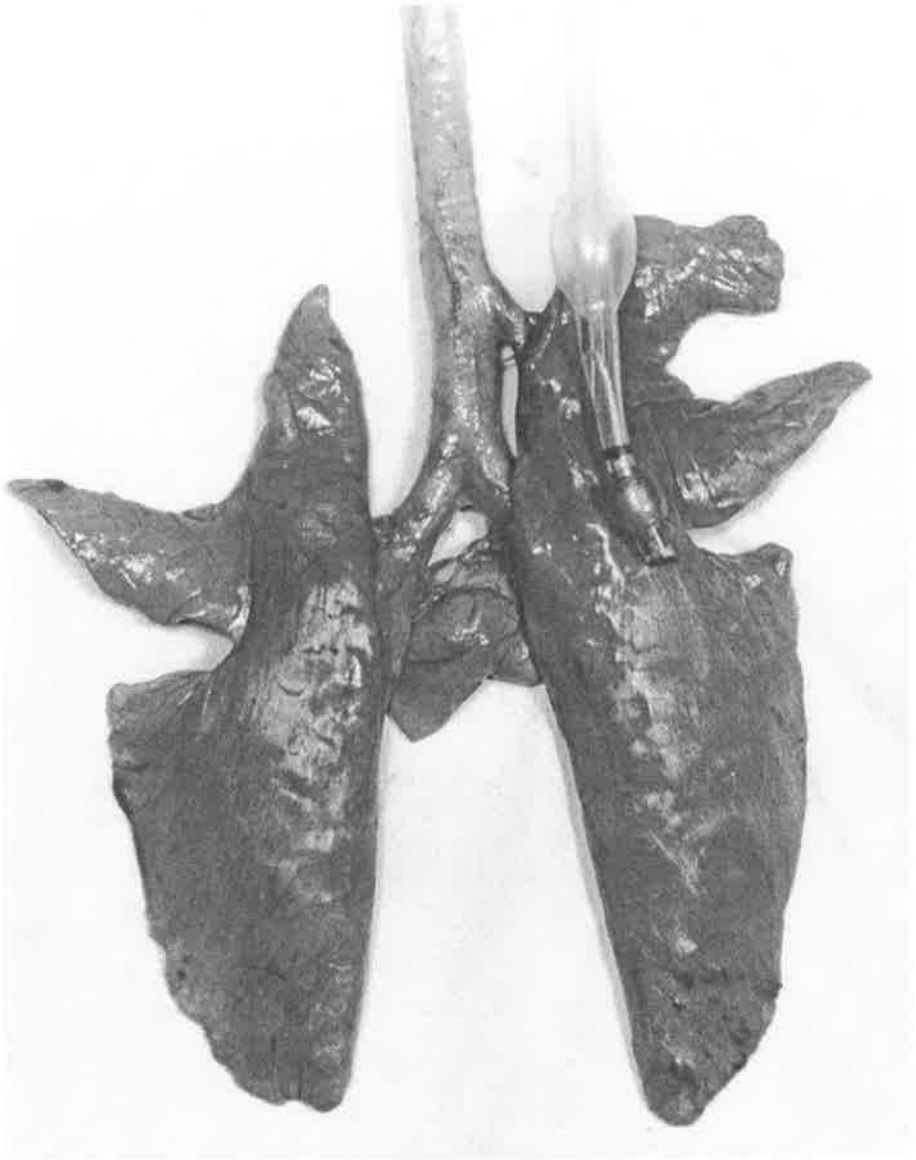

Figure 22 Left tracheal upper lobe bronchus and double lumen tube.

South Australian Domestic White Pig

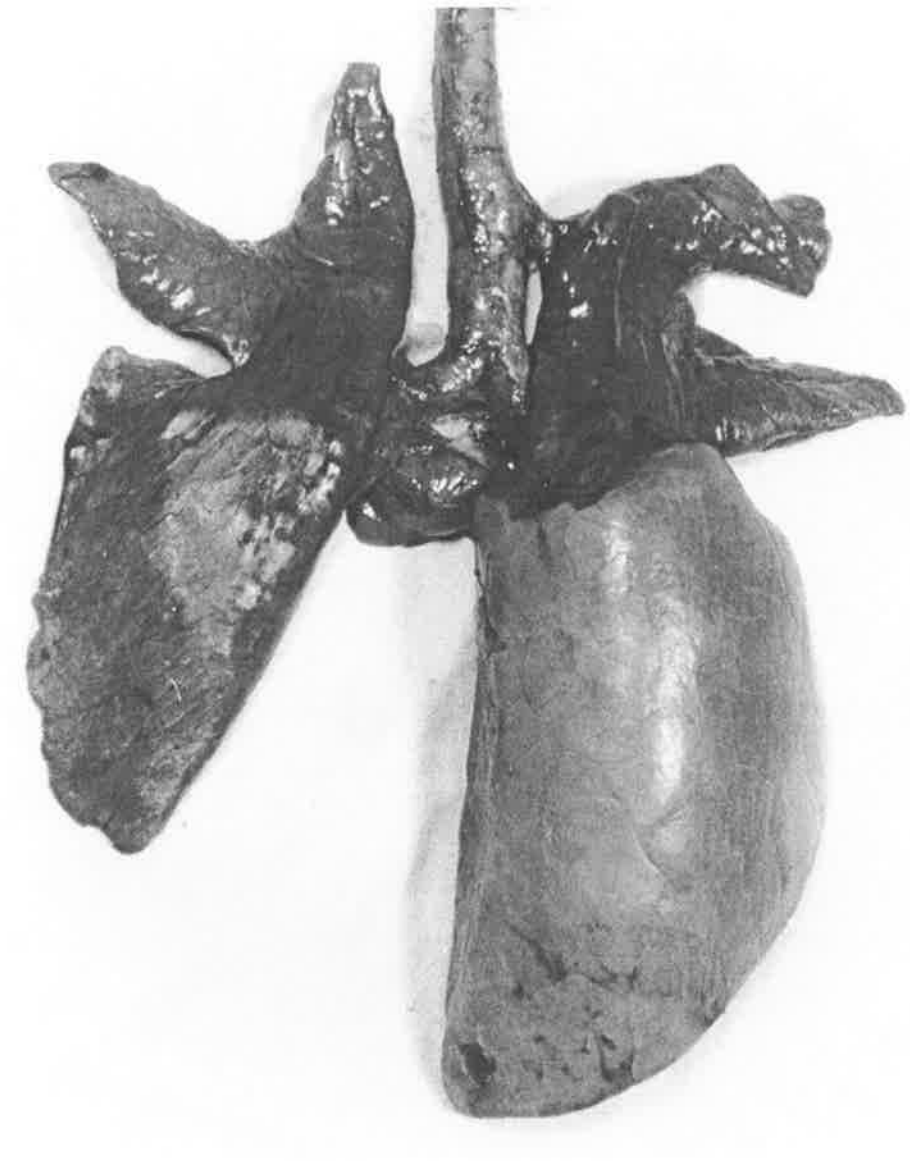

Figure 23 Left single lung ventilation with left tracheal upper lobe bronchus present.

South Australian Domestic White Pig

3.3.3.3 Discussion

The short right and left main bronchi which occur in pigs, and the presence of a lobar (or lobular) bronchus arising from the trachea (Nakakuki, 1994), might be expected to create problems with single-lung ventilation when using commercially available double-lumen tubes designed for human use. The inflated bronchial cuff is likely to unavoidably restrict or obstruct ventilation to major bronchopulmonary segments on the side of the endobronchial intubation, while the inflated tracheal cuff is likely to obstruct or partially obstruct the tracheal bronchus.

In the two pigs that died in the course of single-lung anaesthesia, the tracheal bronchus was on the same side as the endobronchial intubation, an anatomical configuration which was found in three of the six pigs autopsied and which may well be present in other pig populations. Thus, when employing single-lung ventilation in pigs using a double-lumen tube, it should be appreciated that there is very likely to be an upper lobe bronchus originating from the trachea and, furthermore, that it may sometimes not be a right but a left upper lobe bronchus. It is especially important that this latter configuration is identified since the use of a left-sided double lumen tube to ventilate the left lung will result in failure to ventilate a considerable proportion of this lung as well as the whole of the right lung.

This problem could be partly overcome by using fiberoptic bronchoscopy with a paediatric bronchoscope to identify whether the tracheal bronchus is on the right or the left side. Attemps at detecting the specific configuration on chest X-ray were not

successful. Fiberoptic bronchoscopy might also be useful in determining which of the two main bronchi is longer and more suited to accommodating the inflated bronchial cuff. If a left-sided tracheal bronchus is present and the right main bronchus appears longer than the left, it may be better to site the left-sided double-lumen tube electively in the right rather than the left main bronchus.

It can be assumed that although an upper lobe bronchus arising from the trachea will very likely be obstructed or partially obstructed by the inflated tracheal cuff, any ventilation this upper lobe does receive will be from the tracheal and not the bronchial lumen of the double-lumen tube. Whether or not this upper lobe is ventilated will depend upon the particular configuration of the double-lumen tube which has been selected and how this configuration matches the tracheo-bronchial tree anatomy of the particular strain and size of pig being studied. A commercially available double-lumen tube with a long inter-cuff distance will reduce the risk of the inflated tracheal cuff completely obstructing the tracheal bronchus, though if the cuff causes an incomplete but marked obstruction there will be an increased risk of a ball-valve effect resulting in incomplete emptying and hyper-inflation of the upper lobe.

In spite of likely unavoidable obstruction or partial obstruction of an upper lobe bronchus on usually the right side, pigs do survive single-lung anaesthesia. No anaesthetic difficulties were reported in a thoracoscopy study in which fiberoptic bronchoscopy was used to assist placement of the double lumen tube in six pigs (Hill et al, 1996), while in another study using ten pigs no problems were reported

after more comprehensive intra-operative monitoring and intravenous crystalloid infusion were introduced following the death of the first two pigs (Bessell et al, 1994). In our series, the first pig presented no problems during three anaesthetics each lasting three hours. Even the second pig which had a left-sided tracheal bronchus, had an uneventful 3-hour single-lung anaesthetic on the first occasion. Ventilation was with 100% oxygen, and pulse oximetry remained in the high nineties throughout, and it must be presumed that the bronchial cuff of the double-lumen tube obstructed fewer bronchopulmonary segments than it did on the next occasion.

The two pigs that died did so suddenly and unexpectedly, after 80 and 120 minutes of anaesthesia respectively, with good pulse oximetry and end-tidal CO_2 readings. Regrettably, intra-arterial blood pressure was not being monitored, and sensing difficulties with the pulse oximeter on the pig's tail appeared just prior to the terminal event. Death was likely to have been a consequence of low cardiac output and hypoxia; low cardiac output due in part to the high inflation pressures required to ventilate those segments of the left lower lung which were actually being ventilated; and hypoxia from these same high inflation pressures diverting pulmonary blood flow away from the ventilated lung and through the large areas of non-ventilated lung.

As already stated, a paediatric fiberoptic bronchoscope was not available and the double-lumen tube was placed using clinical criteria. Auscultation of the chest to determine the adequacy of upper lobe ventilation was found to be difficult to

interpret at the time. This was due in large part to the relatively narrow upper thorax in the pig, with transmitted breath sounds being pronounced and both sides of the thorax moving with single-lung ventilation. In the first pig with the more usually present right tracheal bronchus, it is likely that both the left and the right upper lobes were obstructed or partially obstructed during the auscultation testing.

Other animal species such as sheep and cattle have similar bronchopulmonary configurations (Nakakuki, 1994), and may also experience problems with single-lung ventilation. Humans, on the other hand, usually have a suitably long left main bronchus, and the incidence of a tracheal bronchus is low. A right tracheal bronchus was identified in only 5 patients in a series of 1,200 consecutive bilateral bronchograms (Atwell, 1996), and in 2% of children requiring bronchoscopy for respiratory symptoms (McLaughlin et al, 1985). When present in humans, a tracheal bronchus is sometimes referred to as a pig bronchus (Measen et al, 1993). The mirror image configuration, with not a right but a left upper lobe bronchus originating from the trachea, is not generally recognised in pigs (Nakakuki, 1994), and is not described in humans (Gubbawy et al, 1984; Lachowicz and Trzebinska-Korniszewska, 1978; Landing and Dixon, 1979; Maesen et al, 1983; Remy et al, 1967). Though its presence in three of six animals studied may reflect an inherited trait peculiar to the particular strain of pigs, it may well be present in other pig populations.

In conclusion, successful single-lung ventilation in pigs necessitates :

1. Fiberoptic bronchoscopy to identify bronchial anatomy and facilitate optimal double-lumen tube placement.
2. Continuous intra-arterial blood pressure monitoring as well as pulse oximetry and end-tidal CO_2 monitoring. Placing the pulse oximeter on a more central and better perfused location, for example the tongue, may also improve monitoring.
3. A fresh gas flow of 100% oxygen both before and during single-lung ventilation in order to minimise the effects of shunting through those areas not being ventilated.

3.3.4. INSTRUMENTS

as described above under section 3.1.3.

3.3.5. STATISTICAL ANALYSIS

A repeated measures analysis of variance was used to assess separate outcome parameters. Gas insufflation with either standard dry gas, warmed humidified gas, or no gas as a control was considered a grouping factor, with time-on-treatment a within-pig factor. An autoregressive error structure was assumed. Program 5V, BMDP Statistical Software, UCLA 1993 was used for analysis. A significance level of 0.01 was adopted.

SECTION 4 RESULTS

4.1. PORCINE LAPAROSCOPY

4.1.1. RESULTS

Using repeated measures analysis of variance, regression lines representing the temperature change over time were fitted to each of the three treatment groups. Because both intraperitoneal and oesophageal temperature changes were concordant in magnitude and direction, oesophageal temperatures only were used to define core temperature changes.

Core temperature was significantly affected by the duration of the experiment and the treatment instituted. The regression lines summarising changes over time for the no gas and heated humidified gas groups showed no statistical differences. Consequently it can be generalised that there was no significant temperature difference between animals that received no gas or heated humidified gas over a 3 hour period, and these two groups can be considered to be indistinguishable.

After 3 hours, core body temperature for control animals that received no gas, and animals that had heated humidified gas insufflated fell by 0.6°C. The core body temperature fall for animals that had cool dry gas insufflated was significantly greater, reaching 1.77°C at 3 hours. The regression line that summarised temperatures recorded by animals undergoing cool dry gas insufflation was significantly different from the pooled estimate of control animals (no gas) and those

receiving heated humidified gas, reaching 1.17°C after 3 hours (Figure 24). Table 1 shows the values recorded by the sensors positioned to instantaneously measure the temperature and relative humidity of insufflated and exsufflated gas. Values were stable over the experimental period, and mean results are displayed. Thermodynamic energy analyses were conducted on these secondary outcome parameters from the cool dry gas insufflation group. The predicted temperature drop due to water evaporation was calculated if a pig of 30 kg is insufflated at a flow rate of 10 L/min for 3 hours assuming that the specific heat capacity of pig tissue is 3.5 kJ/kg, assuming a latent heat of vaporisation of 2.43 J/mg, and assuming a saturated water content at 23.9°C and 31.4°C of 21 mg/L and 33 mg/L respectively. The results confirmed that a large proportion of the temperature drop after insufflation of cool dry gas is due to the latent heat required for evaporation of body water to saturate the dry CO_2 stream, rather than the heat required to raise the cool gas to body temperature. The calculated mean temperature drop due to water evaporation was 1.2°C, which compares with the 1.17°C observed temperature difference between control animals and those insufflated with cool dry gas.

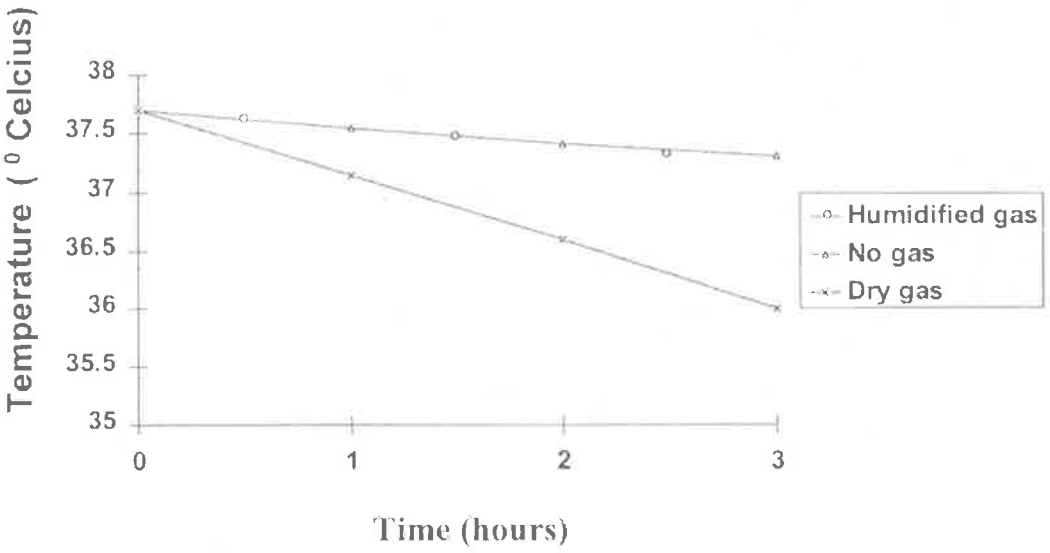

Figure 24 Temperature curve in porcine laparoscopy

Temperature and relative humidity of insufflated and exsufflated gas

	Temperature - in (°C)	Relative humidity - in (%)	Temperature - out (°C)	Relative humidity out (%)
Cool, dry gas	23.9 (21.9 – 25.9)	40.7 (26.1 – 55.4)	31.4 (31 – 31.8)	88.2 (87 – 89.5)
Heated humidified gas	40.7 (39.5 – 42)	98.3 (97.9 – 98.8)	34.5 (34 – 35)	89.4 (87.7 – 91.2)

Values are means accompanied by 95% confidence intervals

Table 1 Results porcine laparoscopy

4.1.2. DISCUSSION

The resurgent interest in laparoscopic visceral surgery that was produced by the technical achievements of the late 1980's also fostered enthusiasm for renewed research into the physiological disturbances caused by the formation of a tension pneumoperitoneum. In less than 10 years, pathophysiological mechanisms have been clearly established by which laparoscopy modifies cardio-respiratory dynamics (Morris and Wilkey, 1970), promotes postoperative hypercoagulability (Morris and Kumar, 1972), diminishes splanchnic visceral blood flow (Conahan, 1982; Laszlo et al, 1990), impairs venous return in lower limb blood vessels (Bessell et al, 1995), and influences many other parameters.

However, in the context of modern operative laparoscopy, temperature is a critical physiological parameter that seems to have escaped rigorous investigation until recently. This is somewhat surprising, as hypothermia (defined as core temperature below 36 degrees Celsius) and its sequelae are frequent perioperative problems with the potential to cause numerous deleterious effects. Conditions such as increased susceptibility to dermal infection (Shanks et al, 1988), induction of a hypokalaemic state (Carli et al, 1989; Schein et al, 1995), impaired myocardial function (Slotman et al, 1985), respiratory depression, negative nitrogen balance (Pike et al, 1996), thrombocytopaenia, and depletion of clotting factors (Beebe et al, 1993) have been associated with perioperative hypothermia. The net effect of these complications is reflected in the mortality rate of patients thus affected. One study reported 24%

mortality in postoperative patients who remained hypothermic after 2 hours compared with 4% of their normothermic counterparts (Flemming et al, 1996). There is also a financial penalty, because hypothermic patients are reported to spend up to 1 hr longer in the Recovery Ward (McDougall et al, 1996), and a mean increase in length of hospital stay of 2.6 days was recently demonstrated for patients with postoperative temperatures less than 35.5°C (Mattheussen et al, 1990).

Before 1995, the literature contained four uncontrolled studies that addressed the issue of laparoscopic hypothermia. Two were from the Georgia Biomedical Research Group, and are the most often cited. The first reported that reduction in core temperature as a result of laparoscopy can be expected to be 0.3°C for each 50 L of CO_2 delivered (Morris, 1971). The second study by the same group reported that postoperative temperatures in 20 patients receiving warmed CO_2 (35-35.5°C) were within 0.1°C of pre- and intra-operative values (Seitzinger and Dudgeon, 1993), although the methodology of this paper has subsequently been questioned (Ludbrook, 1994). Two other studies reported uncontrolled clinical observations of the development of hypothermia during laparoscopic procedures (Clark et al, 1954; Kurz et al, 1996). Since 1993, our group has been trying to more clearly elucidate the physiology of temperature balance during laparoscopy under controlled conditions. The current state of knowledge in this area can be summarised as follows:

1. Mechanisms of hypothermia during general anaesthesia include heat redistribution, disturbance of thermoregulatory mechanisms, and the use of cold intravenous infusions. A major component is heat loss from exposed surfaces, a situation accelerated by a cool theatre environment (Ishizaki et al, 1993; Monagle et al, 1993; Ott, 1991 a and b), evaporation of solutions used for surgical skin preparation, exposed body cavities during surgery (Ott, 1991 b), and the use of cold irrigating fluids (Boelhouwer et al, 1987; Imrie, 1991).

2. Patient characteristics such as age, size and associated medical conditions compound both the degree of hypothermia and also the resultant effects (Ludbrook, 1994).

3. Cool dry CO_2 at 21°C and 0% relative humidity is the standard gas that issues from the patient outlet of the majority of unmodified commercially available insufflators. While some warming and humidification occurs during passage along insufflator tubing, it is apparent that this is minimal, and contributes little to heat conservation.

4. Controlled animal studies have confirmed that insufflation of the standard CO_2 gas supplied with laparoscopic units results in a significant fall in core body temperature, when used at high flow rates over a prolonged period of time (Ludbrook, 1994).

5. Currently available insufflators with built-in heating elements for the warming of insufflated gas confer no protection against laparoscopy-induced hypothermia (Ludbrook, 1994).

6. The intra-abdominal CO_2 during laparoscopic surgery is at body temperature and nearly 100% saturated with body water (Ludbrook, 1994; Sheffield, 1994; Tittel, 1995).

7. The theoretical principles of thermodynamics indicate that considerably more heat expenditure from the patient would be needed to evaporate body water to humidify the initially dry CO_2 stream, than would be required to raise the ambient temperature of the CO_2 gas to body temperature (Ludbrook, 1994).

This study complements and expands our understanding of the mechanisms which control temperature balance during laparoscopy by experimentally confirming the theory that vaporisation of water is a major component of heat loss during laparoscopy, and consequently that humidification of insufflated CO_2 can minimise the problems of laparoscopy-induced hypothermia. Importantly this was achieved simultaneously in two ways, by measuring different outcome parameters.

Firstly the core body temperature changes of animals randomly allocated to different treatment groups were repeatedly measured over a 3 hour period. This cross-over design allowed the examination of only laparoscopy-induced influences on temperature, as heat loss to the environment and anaesthetic circuit were

standardised. Core temperatures after insufflation with heated humidified gas were no different from uninsufflated control animals. This is all the more remarkable considering the deliberately exaggerated gas losses of 10 litres/min in the experimental arm. However, after 3 hours of insufflation with cool dry gas, core temperature dropped by 1.77°C, significantly more than the 0.6°C drop experienced by control animals and those insufflated with heated humidified gas.

Secondly by measuring the temperature and relative humidity of gas entering and exiting the animal model, it was possible to thermodynamically calculate the predicted core temperature fall following insufflation of an animal of 30 kg. In these energy calculations, the component which would be attributed to heating the insufflated CO_2 to physiological levels was ignored because of the extremely low specific heat of gas. The close correlation between the calculated and measured temperature changes in pigs treated with cool dry gas strongly supports the hypothesis that prevention of water loss is the most important factor for the prevention of laparoscopic hypothermia.

Disturbed temperature physiology such as we have demonstrated will not be problematic or apparent in every laparoscopic operation. By far the majority of laparoscopic procedures performed in routine practice are of modest duration and incur minimal gas leakage, and thereby postoperative hypothermia has not proved to be of major clinical significance. However, it is important the clinician utilising non-humidified insufflation equipment be conscious of this potential problem for several reasons:

- Hypothermia can be anticipated if the planned or existing laparoscopic procedure be of prolonged duration and/or incur large gas losses. Complex gastrointestinal procedures such as laparoscopic oesophageal, gastric, colonic or pancreatic resections are examples of such procedures. Appropriate prophylactic measures should be instituted.

- If other factors tending to reduce body temperature during general anaesthesia are present, the magnitude of the hypothermic effect due solely to laparoscopy could exert a clinically significant impact.

- There may be a temptation to submit to commercial pressure to purchase gas-warming insufflators when in fact their touted benefits have no physiological validity.

- Surgeons may assume that the purchase of gas-warming insufflators will protect their patients from hypothermia, perhaps forsaking other precautionary measures.

On the basis of the results of this and previous studies, we advocate the use of warmed and humidified gas to maintain temperature homeostasis during

laparoscopy. At present, however, there are only prototype units that have achieved the certified levels of electrical safety and sterility that could be clinically used.

4.2. LAPAROSCOPIC CHOLE-CYSTECTOMY

4.2.1. RESULTS

The two patient groups were not statistically different in terms of age (23 to 89 years), gender, previous abdominal surgery, performance of intraoperative cholangiography, intraoperative laparoscopic common bile duct exploration, intraoperative given analgesics and narcotics, drain insertion, and time spent in the recovery ward. In no patients were there any abnormalities detected on the perioperative electrocardiogram and all postoperative platelet counts and coagulation indices were within the normal range. In each group there was one minor wound infection.

The mean duration for which pneumoperitoneum was required was 40.0 minutes in the humidified group and 48.3 minutes in the control group. The mean temperature drop during pneumoperitoneum was not significantly different between the groups (0.25° C in the humidified group and 0.3° C in the control group) (Figure 25), despite the humidified group of patients requiring on average 10 litres [L] more CO_2 insufflation (59 L vs 49 L). No adverse effect from the humidification of insufflated gas was observed.

The operating surgeon indicated intraoperative visibility was impaired to a minor degree in one case in each group, notwithstanding initial fogging experienced when the cool lens was introduced into the warm abdominal cavity.

Eight patients (four in each group) were excluded from postoperative pain assessment and follow-up due to conversion to open cholecystectomy, postoperative pancreatitis, or postoperative haematoma formation. The mean postoperative morphine requirement in the group receiving humidified gas was 8.3 mg compared to 17.1 mg in the control group (not statistically significant) (Figure 26). At six hours postoperatively pain assessed by the Analogue Pain Score was significantly reduced in the group following humidified gas insufflation compared to the control group($p=0.02$, $n=32$). Findings were similar on the first ($p=0.03$, $n=27$), second ($p=0.04$, $n=11$), and third postoperative days ($p=0.005$, $n=5$) and also at follow-up ten days after the procedure ($p=0.02$, $n=31$) (Figure 27).

Length of hospitalisation was no different between the two groups (1.5 days in the humidified group and 2.1 days in the control group), however in the humidified group the mean time taken to return to normal activities was significantly less; 5.9 days compared to 10.9 days in the control group ($p=0.04$). Mean time taken to return to work was 9.9 days in the humidified group compared to 14.7 days in the control group ($p=0.13$) (Figure 28).

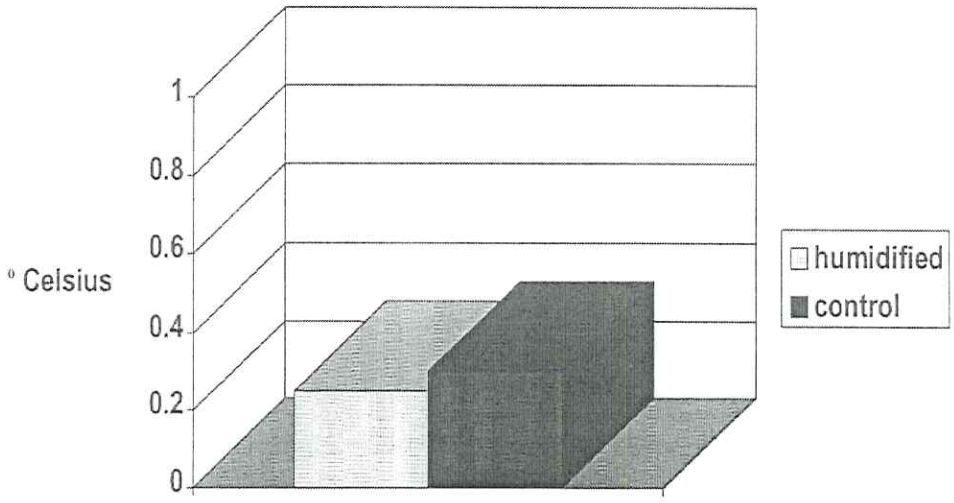

Figure 25 Core temperature drop during humidified and dry gas insufflation in laparoscopic cholecystectomies

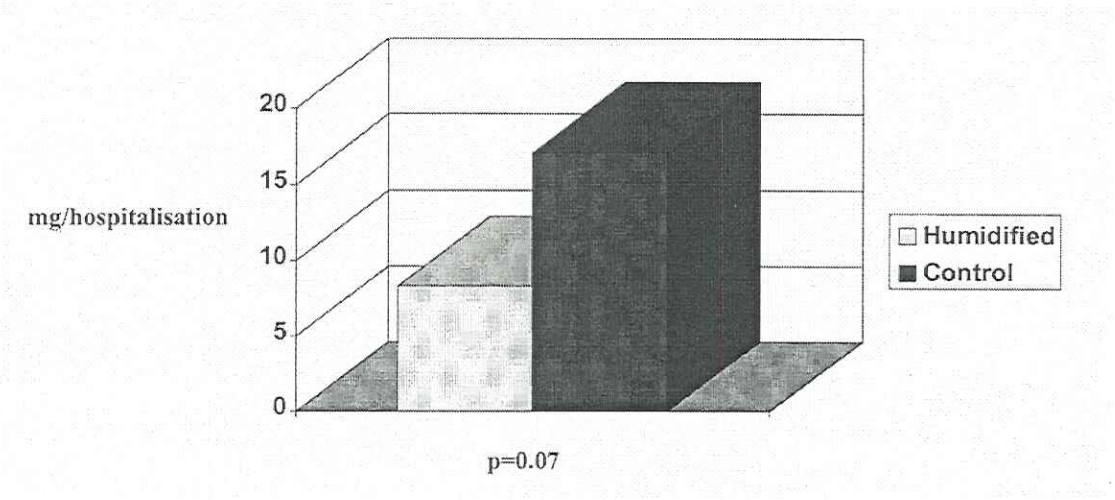

Figure 26 Morphine consumption during hospitalisation after humidified and dry gas insufflation in laparoscopic cholecystectomies

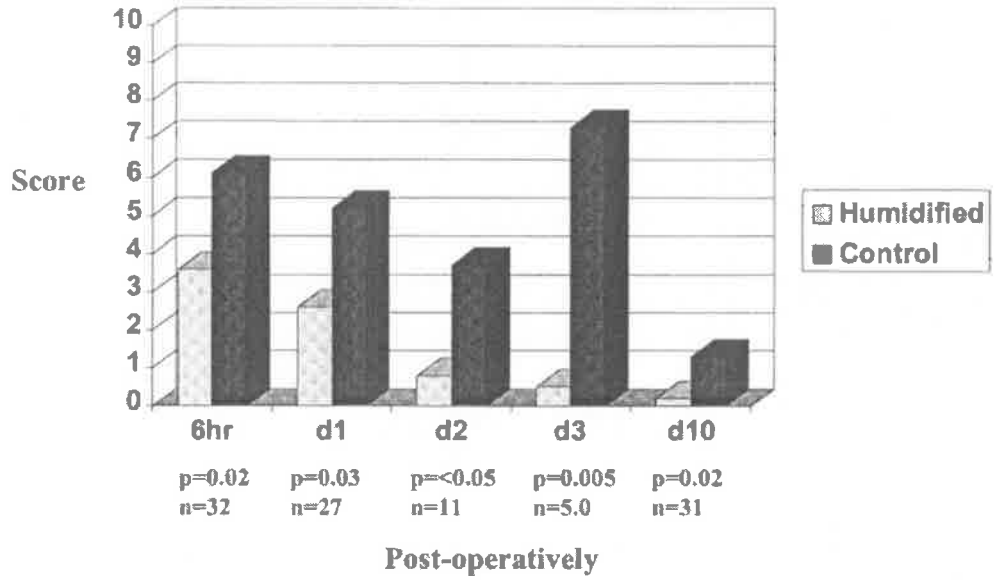

Figure 27 Analogue Pain Scores during hospitalisation after humidified and dry gas insufflation in laparoscopic cholecystectomies

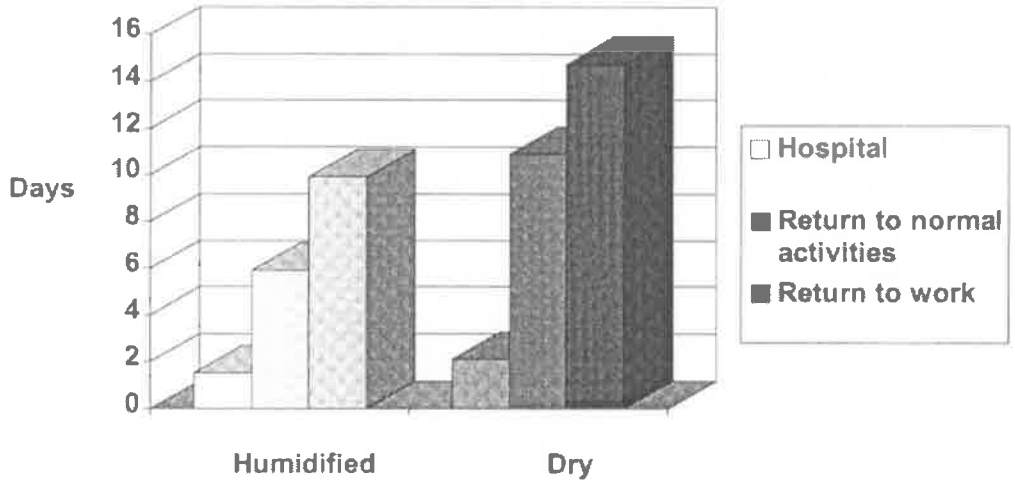

Figure 28 Recovery after humidified and dry gas insufflation in laparoscopic cholecystectomies

4.2.2. ELECTRON MICROSCOPY

Peritoneal biopsies were taken in one patient having humidified gas insufflated and in one patient having dry gas insufflated. The insufflated amount of gas was 52 and 35 liters respectively. In both patients microvilli of the peritoneum were largely intact. The number of intact microvilli slightly decreased with time (Figures 29 and 30). Within this short term procedure with minimal gas consumption no obvious difference between the two types of insufflation gas could be detected.

Figure 29 Electron microscopy of peritoneal surface after one hour of dry gas insufflation

Figure 30 Electron microscopy of peritoneal surface after one hour of humidified gas insufflation

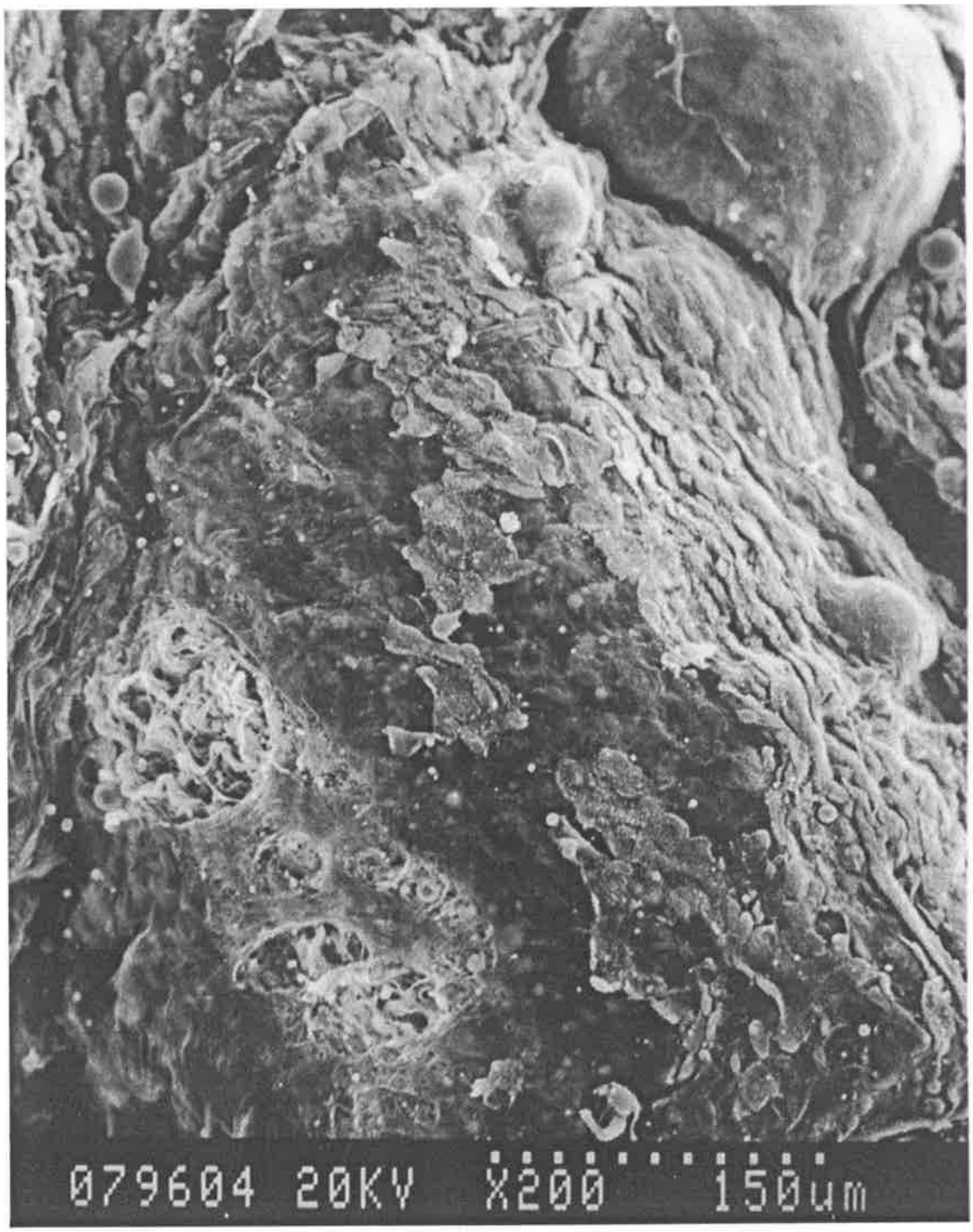

Figure 31 Electron microscopy of peritoneal surface : mechanically damaged basal membrane

4.2.3. DISCUSSION

The experience of this study demonstrated that the use of humidified CO_2 as insufflation gas was straightforward, safe, and required no disruption to the standard operating procedure for laparoscopic surgery. The use of a small humidification chamber incorporated as an integral component of the insufflator line tubing is the only material requirement. This product is currently supplied as a prototype single-use disposable item, and when used with the appropriate insufflator also provides heating capabilities.

The ability of humidified gas insufflation to provide a physiologically thermo-neutral pneumoperitoneum has been proven under exaggerated conditions in animal studies (Bessell and Maddern, 1998), but the practical merit of this facility under normal clinical conditions had been questioned. It appears from this study that for the relatively brief procedure of laparoscopic cholecystectomy, the heat-preserving effect of humidified gas insufflation is not significantly greater than standard dry insufflation gas. However, it is likely to be more pronounced in laparoscopic procedures of prolonged duration and/or where gas losses are large (Bessell and Maddern, 1998). It is therefore suggested that humidified insufflation be used for complex gastrointestinal procedures such as laparoscopic oesophageal, gastric, colonic or pancreatic resections. Humidified insufflation is also recommended when other compounding factors tending to reduce body temperature during general

anaesthesia are present, as the hypothermic effect due to laparoscopy will be exaggerated and could exert a clinically significant effect.

Other results from this study however, provide justification for the use of humidified gas even in brief laparoscopic operations. We demonstrated significantly reduced postoperative pain scores at all measured time intervals in the group that received humidified gas, amongst whom there was a significantly earlier mean time taken to return to normal activities. Compared with patients receiving standard dry insufflation gas, the humidified group also showed a tendency to require less postoperative narcotics along with a shorter period of hospitalisation and earlier return to work, although these results were not statistically significant.

The mechanisms mediating postoperative pain after laparoscopy are considered to be multifactorial (Pier et al, 1994). Cold insufflation gas has been implicated in studies reporting that warm (dry) insufflated gas reduces postoperative pain with an effect lasting up to three days (Korell et al, 1996; Semm, 1994). However in our study the addition of humidification to already warm gas reduced postoperative pain for at least ten days, suggesting humidification may be more important than gas warming. This raises the possibility of ultrastructural trauma to the peritoneum caused by the circulating dry CO_2 gas as a key aetiological factor. Other possible factors influencing post-laparoscopy pain include neuropraxia of the phrenic nerve, lowering of intraperitoneal pH by dissolved CO_2, mechanical peritoneal distension, electro-thermal trauma to the peritoneum, irritation from undrained fluid collections,

retained intraperitoneal gas, and sociocultural and individual factors (Baxter and O'Dwyer, 1995; Berggren et al, 1994; Madsen and Jensen, 1992; Vitale et al, 1991).

It can be concluded that the use of humidified insufflation gas reduces postoperative pain following laparoscopic cholecystectomy, but that for these relatively brief procedures the heat preserving effect of humidified gas insufflation is not significant.

4.3. PORCINE THORACOSCOPY

4.3.1. RESULTS

4.3.1.1. Temperature

The recorded fall in core body temperature of only 0.2 °C after three hours of humidified gas insufflation was significantly less than the fall of 1.9 °C following insufflation of dry gas, and also significantly less than the 1.3 °C temperature drop when no gas was insufflated ($p<0.0001$) (Figure 32). Statistically there were no intergroup differences or changes over time for any of the different physical characteristics of the efferent insufflation gas (humidity, temperature, oxygen saturation, partial pressure of CO_2).

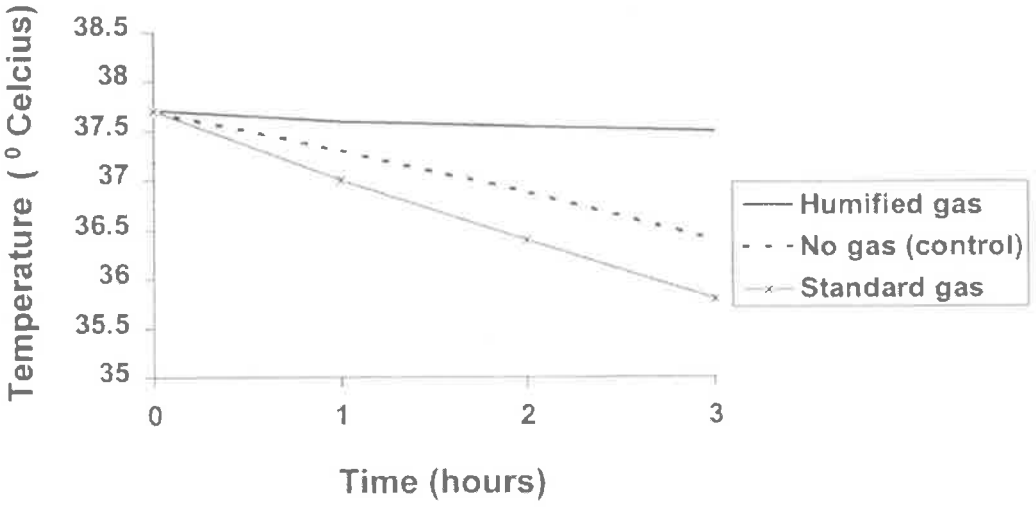

Figure 32 Porcine thoracoscopy : temperature curve after humidified and dry gas insufflation and no insufflation respectively

4.3.1.2. Electron microscopy

The changes which were seen on light microscope histopathological examination of the parietal pleural biopsies depended on whether the particular study was the first, second or third for that animal rather than on the type of gas insufflation. Following the first study in each of the six animals, irrespective of whether it was with humidified, standard dry, or no gas insufflation, normal pleura was seen in all but one examination. In the single exception, acute pleuritis was reported after a first study in which standard dry gas was insufflated. Following the second study acute pleuritis was reported in every animal, and following the third study chronic pleuritis was reported again in every animal.

Electron microscopic examination, however, revealed that even after the first study, the pleural surface sustained ultrastructural destruction of microvilli but only when standard dry gas was insufflated (Figure 33). Such damage was not observed after humidified gas insufflation (Figure 34) or after control studies (Figure 35). Following the second and third procedures the microvilli were destroyed in all animals.

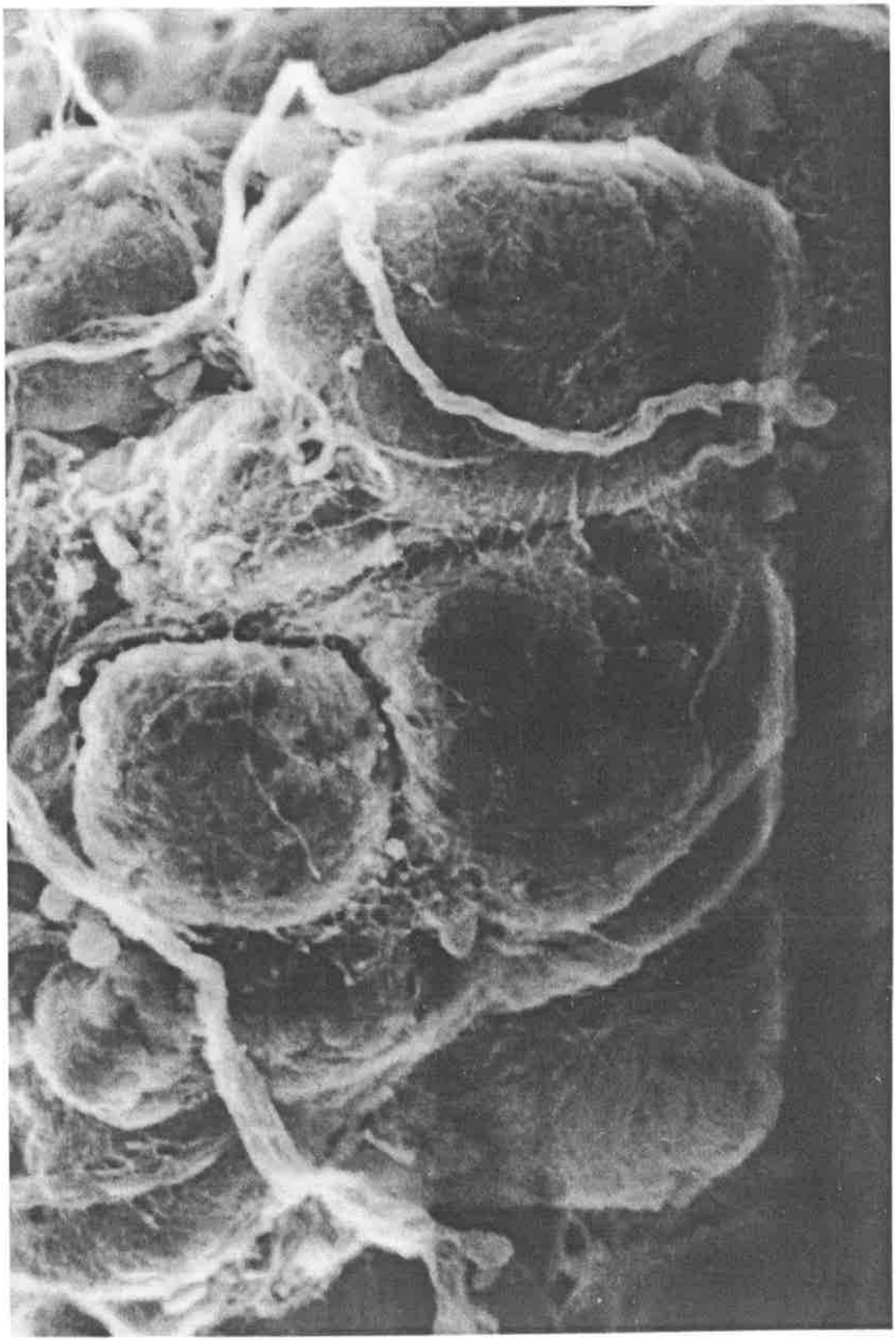

Figure 33 Electron microscopy of pleural surface : after dry gas insufflation

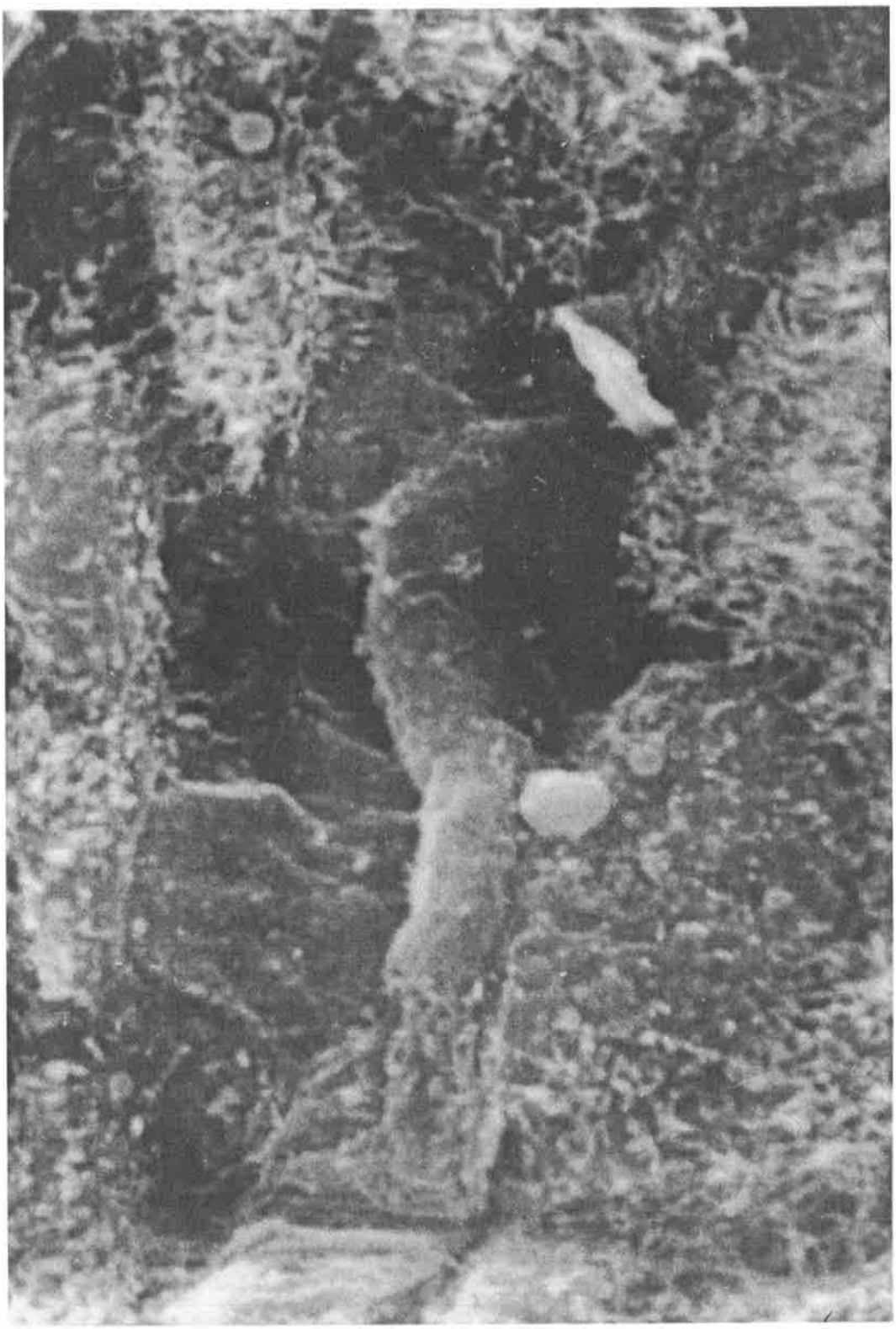

Figure 34 Electron microscopy of pleural surface :
after humidified gas insufflation

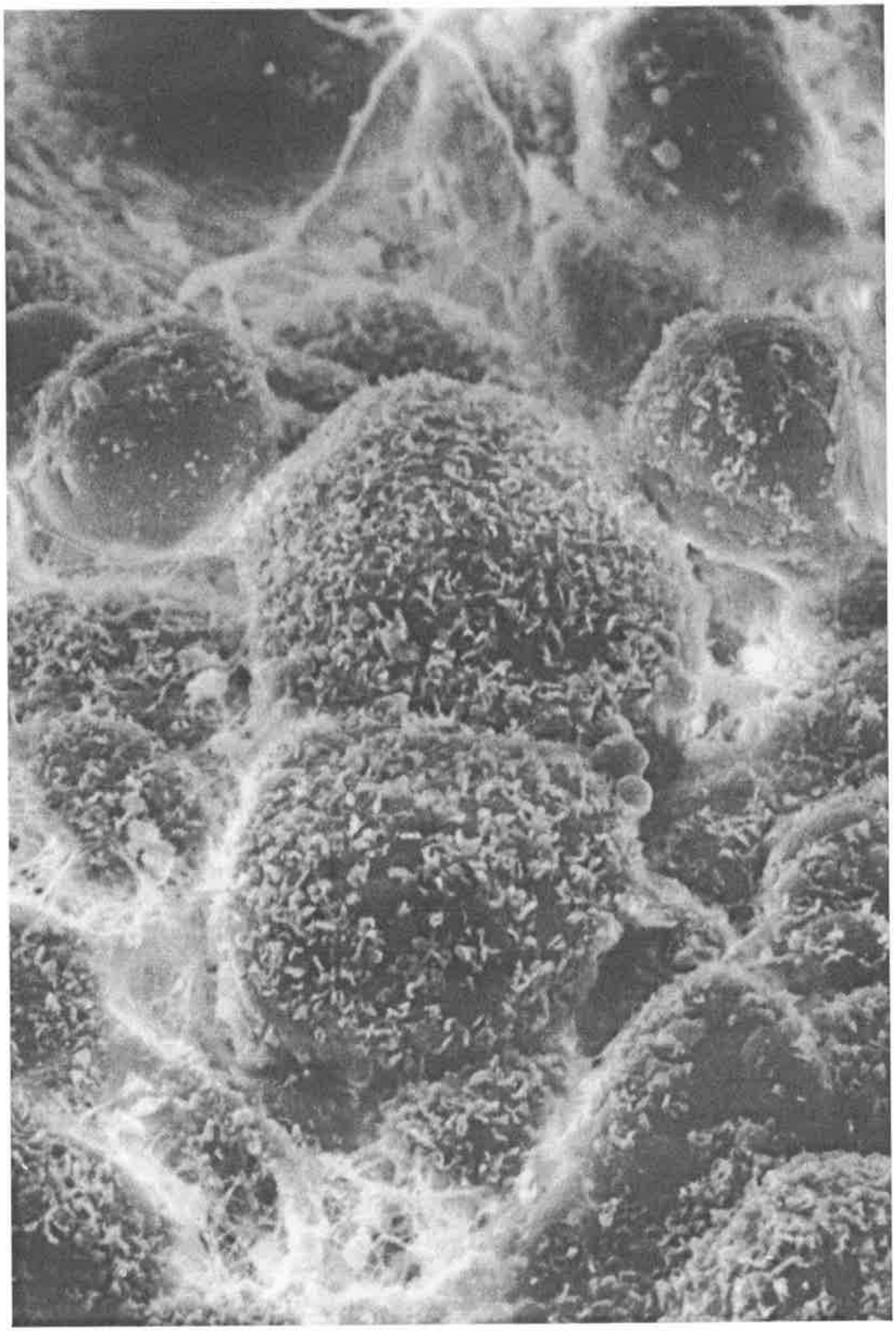

Figure 35 Electron microscopy of pleural surface :
after no gas insufflation

4.3.1.3. Supplementary Results

At the time that the thoracoscopic ports were being sited surgically, it was observed at the second study on each animal that there was clinical evidence of minor wound inflammation or infection in relation to the incisions performed the week previously. At the third study pleural adhaesions were present in each animal.

At autopsy following the conclusion of the third treatment, all pigs were found to have an upper lobe bronchus originating from the trachea. In three it originated from the right side of the trachea, and in three from the left.

4.3.2. DISCUSSION

The use of humidified insufflation gas has to date only been applied during laparoscopic procedures in animal studies and human clinical trials, with potential benefits being the prevention of perioperative hypothermia and reduced levels of postoperative pain (Bessell et al, 1995; Bessell and Maddern, 1998). Since gas insufflation is also used in many centres during thoracoscopy to facilitate collapse of the lung on the side of operation (Coltharp et al, 1992; Giudicelli et al, 1994; Landreneau et al, 1992; Lewis et al, 1995), it seems logical to assess whether the same advantages might apply.

The present study looked only at the temperature preserving effects and histological changes produced by the insufflation of humidified CO_2 as compared to dry CO_2 and to no insufflation. The insufflation was performed at near ambient pressure since insufflation at pressures of more than 5 mm Hg is not recommended during thoracoscopy (Hill et al, 1996; Jones et al, 1993; Wolfer et al, 1994). The cross-over design of the study and the controlled methodology has been previously described (Bessell et al , 1995; Bessell and Maddern, 1998). It allowed the examination of only the thoracoscopy-induced core temperature changes, since respiratory and environmental heat losses were standardised.

The appreciable fall in core body temperature seen in the control studies was the result of the disruption with general anaesthesia of the thermal regulatory mechanisms (Sessler, 1997). The fall was further accentuated by the use of a standard 5 L/min flow of cold dry insufflation gas, with core body temperature being lowered by almost 2 °C. This is a consequence of the rapid warming and humidification to 90% saturation of gases introduced into a body cavity (Bessell and Maddern, 1998), with loss of body heat predominantly as latent heat of vaporisation.

On the other hand, after 3 hours of insufflation at 5 L/min of CO_2 which was warmed to 38.6°C and actively humidified to between 86% and 99%, a temperature drop of only 0.2 °C was observed. This indicates a significant heat-preserving or warming effect which can only be attributable to the use of humidified insufflation.

It remains to be proven whether humidified gas insufflation during thoracoscopy has a temperature-preserving effect in the clinical setting, thereby reducing the risk of hypothermia and its possible sequelae (Slotman, 1985) such as prolonged recovery (Conahan, 1982) and lowered resistance to wound infection (Sheffield, 1994). It also remains to be proven whether the use of humidified gas insufflation will reduce the level of postoperative pain. Pain following thoracoscopy inhibits deep breathing and coughing, so predisposing to sputum retention, atelectasis, pneumonia and prolonged hospital stay. It is multifactorial in origin with contributing factors being the division and re-approximation of respiratory muscles and periosteal and pleural irritation caused by the chest drains. Another factor may be a physical injury to the sensitive parietal pleura induced by dry gas insufflation. The electron microscopy assessment of the ultrastructural changes occurring in this study suggests that standard dry gas insufflation is responsible for a greater insult to the parietal pleura than is caused by humidified gas insufflation (Gaudio et al, 1988; Peng et al, 1994). This supports the hypothesis that humidification of insufflated gas may reduce postoperative pain.

The use of a single lumen endotracheal tube in animals 4, 5 and 6 does not detract from the value of the study. Although double lumen endobronchial tubes are usually employed during thoracoscopy to facilitate lung collapse, some centres for certain operations routinely use CO_2 insufflation and a single lumen endotracheal tube (Olsfanger et al, 1995). The reason for changing to an endotracheal tube was the presence, as an unpredictable complication, of an upper lobe bronchus originating from the trachea on the left side. While an upper lobe bronchus originating from the

right side is well recognised in pigs, (Hill et al, 1996; Jones et al, 1993; Mount and Ingram, 1971; Nakakuki, 1994; Swindle et al, 1986) the left-sided anatomical variation has not been previously described.

It is concluded that in pigs dry gas insufflation during thoracoscopy results not only in loss of body heat but also in physical inflammatory injury to the parietal pleura which could conceivably result in an increase in the level of postoperative pain. Humidification of the insufflated CO_2 during thoracoscopy has the potential to overcome these problems and is considered safe to be evaluated in a clinical trial.

SECTION 5 SUMMARY AND CONCLUSIONS

A first experimental study evaluated whether humidification of warmed insufflated CO_2 during laparoscopic procedures would resolve the problem of laparoscopy-induced hypothermia.

Core temperature changes in 5 anaesthetised pigs were measured over a 3 hour period. Animals were randomly allocated to insufflation at 10 L/min with either cool dry CO_2 gas, heated humidified CO_2 gas, or no gas. Each animal was therefore studied on 3 separate occasions, acting as its own control. The order of these treatments was randomised and performed one week apart to allow the animal to recover from the anaesthetic. Oesophageal temperatures were the primary outcome parameters measured at fifteen minute intervals by thermoresistors.

Using repeated measures analysis of variance, regression lines representing the temperature change over time were fitted to each of the three treatment groups. Because both intraperitoneal and oesophageal temperature changes were concordant in magnitude and direction, oesophageal temperatures only were used to define core temperature changes.

Core temperatures after insufflation with heated humidified gas were no different from controls. After insufflation with cool dry gas, core temperature dropped by 1.77 °C, significantly more than the 0.6°C drop experienced by control animals and those insufflated with heated humidified gas ($p < 0.01$).

Thermodynamic calculations of the heat expended in evaporation of water were also

performed. The temperature drop due to water evaporation alone in pigs insufflated with cool dry gas was calculated to be 1.2°C. This compares favourably with the measured 1.17°C temperature difference between these animals and the control group.

These results confirm that the majority of heat lost during laparoscopic insufflation is due to water evaporation, and this can be prevented using heated and humidified insufflated gas.

Then followed a randomised controlled trial conducted during laparoscopic cholecystectomy to determine the extent of heat preservation and postoperative pain reduction using humidified carbon dioxide (CO_2) gas insufflation instead of standard dry insufflation gas.

Forty consecutive patients were randomised. Twenty patients received humidified CO_2, and twenty control patients received standard CO_2 insufflation. In the group receiving humidified gas, the insufflator tubing incorporated a humidification chamber to generate relative humidity of 88 to 90%. In the group receiving standard dry insufflation gas no such humidification chamber or insulated heating coil were incorporated in the afferent insufflator tubing, thereby delivering gas at a temperature of 21.2 to 25.2^0 C and relative humidity 0.0 to 5.0 % to the patient. The operation was performed using a standardised four port technique by seven different

surgeons. Standardised routine general anaesthesia was administered by eleven different anaesthetists.

The two patient groups were demographically similar and specifically in terms of age (23 to 89 years), gender, previous abdominal surgery, performance of intraoperative cholangiography, intraoperative laparoscopic common bile duct exploration, intraoperative given analgesics and narcotics, drain insertion, and time spent in the recovery ward. No adverse effect from the humidification of insufflated gas was observed. There was no significant difference in core body temperature between the two groups for this brief operation. Pain assessed by the Analogue Pain Score was significantly reduced in the group following humidified gas insufflation compared to the control group at six hours postoperatively as well as on the first, second, and third postoperative days and also at follow-up ten days after the operation. In the humidified group the mean time taken to return to normal activities was significantly less; 5.9 days compared to 10.9 days in the control group. The operating surgeon indicated intraoperative visibility was impaired to a minor degree in one case in each group, notwithstanding initial fogging experienced when the cool lens was introduced into the warm abdominal cavity.

The use of humidified insufflation gas reduces postoperative pain following laparoscopic cholecystectomy, but for these relatively brief procedures the heat preserving effect of humidified gas insufflation is not significant.
The humidification of gas insufflated during laparoscopy can reduce the degree of postoperative hypothermia and may result in less peritoneal reaction and less

postoperative pain. This next study was designed to determine whether these beneficial effects of humidified gas insufflation applied also to thoracoscopy.

Six pigs were each studied on three separate occasions with insufflation into the right thoracic cavity of either humidified gas, standard dry gas, or no insufflation as the control procedure. The studies were performed under general anaesthesia following placement of either a left-sided double-lumen endobronchial tube or an endotracheal tube. This latter tube was used in preference to the double-lumen endobronchial tube since two animals died during the procedure. At autopsy both pigs were found to have the left upper lobe originating from the trachea, thus making single lung ventilation of the left lung for long periods extremely hazardous due to the risk of hypoxaemia and subsequent myocardial infarction. Two 10 mm thoracoscopy ports were inserted via the right 4th and 5th intercostal spaces anterolaterally. Core body temperature and temperature and relative humidity of both the insufflated and the exiting gases was recorded every 15 minutes and biopsies of the parietal pleura were taken at the end of each study for electron and light microscopy.

The recorded fall in core body temperature of only 0.2 °C after three hours of humidified gas insufflation was significantly less than the fall of 1.9 °C following insufflation of dry gas, and also significantly less than the 1.3 °C temperature drop when no gas was insufflated ($p<0.0001$). Electron microscopic examination revealed that after the first study, the pleural surface sustained ultrastructural destruction of

microvilli only when standard dry gas was insufflated . Such damage was not observed after humidified gas insufflation or after control studies. Following the second and third procedures the microvilli were destroyed in all animals.

It can be concluded therefore that the potential benefits of humidifying insufflation gas during thoracoscopy warrant its evaluation in the clinical setting.

In summary the insufflation of humidified gas during laparoscopy and thoracoscopy may have a body temperature preserving as well as a post-operative pain reducing effect. Ultrastructural studies suggest that physical trauma to the peritoneum and pleura is less when humidified rather than dry gas is insufflated. No adverse effects of humidified gas insufflation were seen.

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