LAPAROSCOPIC INTERVENTIONS IN DOGS: PHYSIOPATHOLOGICAL CHANGES AND THEIR IMPACT ON THE PATIENT

Laparoscopische interventies bij honden: fysiopathologische veranderingen en hun invloed op de patiënt

L. Weiland ¹, I. Polis ², H. de Rooster ², F. Gasthuys ¹

¹ Department of Surgery and Anesthesiology of Domestic Animals ² Department of Small Animal Medicine and Clinical Biology Faculty of Veterinary Medicine, Ghent University Salisburylaan 133, B-9820 Merelbeke, Belgium lindaweil@hotmail.com

ABSTRACT

In recent years, laparoscopic surgery in veterinary medicine has become a more common clinical practice. It has been applauded because of its obvious benefits: less tissue trauma, fast healing, less postoperative pain and consequently less postoperative care. This minimally invasive surgery can however lead to serious physiological changes and complications. In this review, the advantages of laparoscopy and the side-effects of the anesthesia are analyzed. The major problems encountered during laparoscopic surgery are related to the cardiopulmonary effects of the pneumoperitoneum, systemic carbon dioxide absorption, extraperitoneal gas insufflation and venous gas embolism.

Appropriate anesthetic equipment to monitor the patient is necessary, as it allows the anesthesiologist to recognize and treat eventual complications. An understanding of the basic pathophysiology of laparoscopy is required before dealing with the individual problems of the patient. The surgeon should be adequately trained before undertaking any surgical procedure with a laparoscope.

SAMENVATTING

De laatste jaren worden meer en meer laparoscopische ingrepen uitgevoerd in de diergeneeskunde. De laparoscopie wordt toegejuicht omwille van zijn vele voordelen: minder weefseltrauma, sneller wondherstel, minder postoperatieve pijn en bijgevolg ook minder postoperatieve zorgen. Deze minimaal invasieve chirurgische techniek kan echter aanleiding geven tot ernstige fysiologische veranderingen en complicaties. In dit overzicht worden de voordelen en neveneffecten tijdens de anesthesie besproken. De meest uitgesproken problemen tijdens laparoscopie zijn gerelateerd aan de cardiopulmonaire effecten te wijten aan het pneumoperitoneum, de systemische CO₂-absorptie, de extraperitoneale gasinsufflatie en het risico op veneuze gasembolie. Aangepaste anesthesiemonitoring van de patiënt is noodzakelijk om eventuele complicaties zo vlug mogelijk te herkennen en te behandelen. Enig begrip van de pathofysiologie tijdens laparoscopie is vereist om specifieke problemen van de patiënt te onderkennen. Ook moet de chirurg voldoende ervaring hebben om de laparoscopie snel en correct uit te voeren.

INTRODUCTION

The first documented laparoscopy on a live, anesthetized dog was performed by Georg Kelling, a human surgeon from Dresden, in the year 1901 (Lindberg, 2002). Major improvements in the optical system and the introduction of the video laparoscope in 1986 made endosurgery really popular (Williams

and Murr, 1993; Siegl *et al*, 1994). Nowadays many diagnostic procedures and surgeries are performed laparoscopically in dogs. Laparoscopy enables the surgeon to inspect a large number of abdominal organs: gall bladder, kidneys, pancreas, ovaries and liver (Richter, 2001). The small size of the wound and the consequent reduction in tissue trauma ensure a quick and uneventful recovery. The patient needs less post-

operative care, fewer analgesic drugs and no Elizabethan collar. There is no contraindication to doing exercise after the intervention, and both animal and owner seem satisfied. In recent years many veterinarians have recognized the advantages of this non-invasive technique and laparoscopic surgery has become a more common procedure in veterinary medicine. However, there are some serious side effects that may occur during anesthesia which can make this non-invasive surgery a potentially high risk intervention. The anesthetic problems inherent in the endoscopic technique are discussed in this review.

BASICS OF LAPAROSCOPIC TECHNIQUE

Minimally invasive surgery requires adequate visualization and access to abdominal structures. Therefore a pneumoperitoneum is established by abdominal insufflation of carbon dioxide (CO₂), air, helium or nitrous oxide (N₂O) (Iberti *et al*, 1987). This can be done in two ways: a closed technique with a Veress needle or an open technique with a Hasson trocar.

The Veress needle contains a spring-loaded, hollow, blunt obturator inner portion and a stopcock (Richter, 2001). The blunt obturator prevents abdominal organ trauma, while the outer cannula with a sharp point makes the penetration of the abdominal wall easier.

In the open technique, a periumbical incision is made down to the periumbical cavity under direct vision. A Hasson trocar is inserted and used to instill gas through its cannula.

The pneumoperitoneum is established by gas passing through the obturator into the abdomen. Gas (usually CO₂) is insufflated intraperitoneally until an intra-abdominal pressure of maximally 15 mm Hg has been reached (Richter, 2001). A laparoscope is inserted through the cannula. Either the surgeon looks directly through the eyepiece or attaches a video camera. This allows the viewing of the operation field on a monitor. Working instruments such as an electrocauter, biopsy needles, graspers, and scissors are introduced in the abdomen at secondary ports (Richter, 2001).

INSUFFLATION GASES

The ideal insufflation gas should be transparent, colorless, non-explosive, physiologically inert; it is neither absorbed nor eliminated by the pulmonary system (Kolata and Freeman, 1999). Several different gases have been tested and carbon dioxide is nowadays the gas of choice for current clinical application.

Unlike nitrous oxide or air, it does not support combustion and can therefore be used with electrocautery. CO₂ is more soluble than the other insufflation gases, hereby decreasing the risk for gas embolism; furthermore it is rather inexpensive. The adverse effects of CO₂ are peritoneal irritation due to formation of carbonic acid and its absorption into the blood, possibly leading to hypercapnia with ensuing stimulation of the sympathetic nervous system (hypertension, tachycardia, arrhythmias), vasodilatation and metabolic acidosis (Williams and Murr, 1993). Under anesthesia, positive pressure ventilation is necessary in order to maintain normocapnia.

N₂O has analgesic properties and gives less peritoneal irritation than CO₂, but it is highly inflammable and precludes the use of electrocoagulation (Wolf *et al*, 1994, Duke *et al*, 1996). Moreover, it can lead to distension of hollow viscera containing nitrogen, and may cause diffusion hypoxia during recovery. The inert gases (helium, argon and xenon) have similar advantages as nitrous oxide, but are more expensive and induce a higher risk of gas embolism.

Air and oxygen are never used nowadays. These gases are explosive and can promote air embolus because of their low blood solubility.

MAIN SIDE EFFECTS OF PNEUMOPERITONEUM

The normal intraperitoneal pressure in man varies from -5 to +7 mm Hg with an average of +2 mm Hg (Iberti *et al*, 1987). An increase in elevated intra-abdominal pressure (IAP) causes important cardiovascular, pulmonary and renal changes.

A decrease in cardiac output by reduction of venous return and higher afterload due to increased peripheral resistance can be expected when the intra-abdominal pressure goes up to 40 mm Hg. This has been confirmed in several studies (Ivankovich *et al*, 1975; Kashtan *et al*, 1981; Williams and Murr, 1993; O'Malley and Cunningham, 2001). On the other hand, the study of Duke *et al* (1996) showed no significant change in cardiac output during an intra-abdominal pressure of 15 mm Hg. An initial so-called paradoxical increase in cardiac output has also been reported in man. This phenomenon was explained by the reduction of blood volume in the splanchnic vasculature and redistribution to the central compartment (Richardson and Trinkle, 1976; Chui *et al.*, 1993).

The high pressure in the abdomen causes a cranial shift of the diaphragm towards the thoracic cavity, which leads to an increase in intrathoracic pressure. The elevated IAP tends to increase physiological

dead space and reduce compliance, leading to a decrease in functional residual capacity and a ventilation-perfusion mismatch. The cranial movement of the diaphragm enhances the formation of atelectasis, which can decrease the oxygenation of the patient. Perioperative hypoxemia can occur if gas mixtures with a low O₂ fraction (e.g. FiO₂ 30% to 40%) are administered (Duke, 1996). These changes are more pronounced in patients with cardiac or pulmonary diseases. A capnogram is useful for measuring end-tidal CO2 in anesthetized patients, but end-tidal CO2 may not always reflect accurately the ventilation status. A periodic arterial blood gas analysis is certainly justified in patients undergoing laparoscopy. When CO₂ is used as abdominal insufflation gas, the arterial partial pressure of carbon dioxide (PaCO₂) usually increases due to transperitoneal absorption of CO2. Hypercarbia and associated respiratory acidosis can be controlled by increasing the minute ventilation during intermittent positive pressure ventilation (Duke et al, 1996). Subcutaneous or retroperitoneal insufflated CO2 is absorbed faster than intraperitoneal CO2 (Koivusalo and Lindgren, 2000). No change occurred in PaCO2 when the insufflation gas was helium (Leighton et al, 1992) and N2O (Ivankovich et al, 1975).

Oliguria is a common observation during laparoscopy in man. When the IAP pressure increases to 20 mm Hg, the renal vascular resistance increases by 555 % and the renal glomerular filtration rate decreases by 25 % (O'Malley and Cunningham, 2001). The compression of the abdominal vena cava, on the one hand, and the increase in the ADH level, on the other, are the possible causes of decreased urinary output (Koivusalo and Lindgren, 2000; O'Malley and Cunningham, 2001). Anuria has also been reported in dogs with an IAP up to 40 mm Hg (Bailey and Pablo, 1999).

OTHER CARDIOPULMONARY RISKS OF PNEU-MOPERITONEUM

Venous gas embolism is a severe complication that can occur during laparoscopy (Wolf et al, 1994). There is a risk of puncturing the venous system through an inappropriate use of the Veress needle. Tension pneumoperitoneum can also force gas into an injured vessel. Even more importantly, high intra-abdominal pressures (20 to 40 mm Hg) favor the formation of gas emboli. The solubility of the insufflated gas is the most significant factor: a low solubility is accompanied by a higher risk for emboli (Wolf et al, 1994). Small amounts of gas provoke few problems, while large amounts of gas bubbles can reduce or even stop

the flow of blood towards or in the heart. Death occurs because an "airlock" is created in the right atrium and ventricle and the pulmonary arteries with a consequent obstruction of the pulmonary flow. This "airlock" results in reduced venous return with a decrease in cardiac output and a subsequent acute right heart failure (Chui et al, 1993). This phenomenon can be diagnosed by a typical mill-wheel murmur on auscultation, a suddenly occurring hypoxemia (low peripheral oxygen saturation) and systemic hypotension and a decrease in end tidal CO₂ (Bailey and Pablo, 1999; Gilroy and Anson, 1987). The characteristic millwheel murmur is a crunching sound caused by the right ventricle beating against the air bubbles. Treatment should be immediate and includes discontinuation of insufflation together with a CPR and the placement of a central venous line to try to aspirate the accumulated gas (Gilroy and Anson, 1987).

Gas can accidentally be insufflated outside the peritoneal cavity, which can lead to subcutaneous emphysema. The subcutaneous or subfascial emphysema usually resolves after 24 hours. Due to possible existing small defects in the diaphragm which have gone unnoticed, the gas can enter pleural and pericardial spaces causing pneumothorax, -mediastinum and -pericardium. The consequent pneumothorax can induce hypoxemia, tachypnoe and tachycardia with hypotension. An appropriate therapy for pneumothorax involving a one-way Heimlich valve is indicated.

Arrhythmias such as sinus bradycardia and even asystoly can occur due to a vagal stimulation induced by a fast intra-abdominal insufflation.

INFLUENCES OF POSITIONING

During endoscopic surgery the surgical table is tilted to allow a better view of the area of interest. Patient positioning during laparoscopy has major effects on most hemodynamic parameters. During the classic Trendelenburg position (30° head down), abdominal organs slide cranially allowing a better view of the caudal abdominal cavity. This position is accompanied with an increased pressure on the diaphragm inducing changes in pulmonary mechanics and cardiovascular parameters. Heart rate generally remains constant, but cardiac output decreased significantly in men and dogs (Bailey and Pablo, 1999). A15° of the head-down positioning in anesthetized dogs was demonstrated to have less impact on cardiac output while using an IAP of 15 mmHg (Williams and Murr, 1993).

During the reverse Trendelenburg position (30° head up), abdominal organs slide caudally allowing a

Table 1. Influences of positioning on cardiopulmonary parameters during laparoscopy in dogs.

TRENDELENBURG POSITION **INCREASE DECREASE** Mean arterial blood pressure Functional residual capacity Mean pulmonary arterial pressure Pulmonary compliance Pulmonary shunt fraction Vital capacity Cerebral venous, spinal fluid pressure Stroke volume Vascular resistance Index of cardiac contractility Minute ventilation REVERSE TRENDELENBURG POSITION **INCREASE DECREASE** Heart rate Cardiac output Cerebral vascular resistance Mean arterial blood pressure Minute ventilation Vital capacity

better view of the cranial area of the abdomen. A significant decrease in cardiac output and stroke volume was observed in men and dogs due to venous pooling, along with a significant decline in preload (Williams and Murr, 1993; Duke, 1996; O'Malley and Cunningham, 2001) (Table 1).

SPECIFIC ASPECTS OF THE ANESTHETIC PROTOCOL FOR LAPAROSCOPIC PROCEDURES

A careful examination should precede any laparoscopic intervention. Coexisting diseases such as diabetes mellitus or hyperthyroidism should be treated preoperatively. Patients with a diaphragmatic hernia or with infections of the abdominal wall should not be scheduled for surgery.

The cardiovascular changes that are induced by the pneumoperitoneum should be taken into consideration when choosing an anesthetic protocol.

Alow dose of phenothiazines (such as acepromazine) induces moderate sedation and muscle relaxation. However, these neuroleptics are accompanied by an

alpha-lytic effect (dose dependant vasodilatation), which may intensify the cardiovascular changes associated with laparoscopy. Alpha-2 agonists (including xylazine and medetomidine) produce analgesia, muscle relaxation and sedation. These drugs reduce cardiac output significantly and increase pulmonary and systemic vascular resistance. Therefore the cardiovascular side effects that occur do not justify the use of alpha-2 agonists in laparoscopic procedures. Postoperative pain can be minimized by analgesics if they are given before surgical manipulation (preemptive analgesia). Analgesia can be provided by opioids, local anesthetics or nonsteroidal anti-inflammatory agents, whether administered alone or in combination. The effects of opioids on the cardiovascular system are minimal (Martin, 1983); a clinically relevant respiratory depression is rarely observed in patients, except for the potent opioids, including fentanyl, sufentanil and alfentanil (Nolan and Reid, 1991, Hall et al, 2001). Induction can be performed either with thiopental or propofol. Propofol was proven to induce a reduction in the size of the spleen compared to thiopental, decreasing accidental puncturing of the spleen during the placement of the trocar (Wilson *et al*, 2004).

The maintenance of anesthesia for laparoscopy is generally performed with an inhalent agent such as isoflurane, sevoflurane and desflurane. Supplemental analgesia is provided preoperatively by an opioid such as fentanyl or sufentanil, either given as a continuous rate infusion or administered in boli (Martin *et al*, 2001). Nitrous oxide is not recommended as there is little MAC reduction compared to men and it leads to low inspired oxygen concentration. Moreover, nitrous oxide diffuses into viscera containing nitrogen, distending hereby the intestines and interfering with the laparoscopic field.

Local and regional anesthesia, such as epidural anesthesia with lidocaine or bupivacaine, help to provide supplemental analgesia and are attractive for postoperative pain management (Bailey and Pablo, 1999).

Neuromuscular blocking agents help to maximize abdominal distension while minimizing intra-abdominal pressure (Chui *et al*, 1993, Bailey and Pablo, 1999). Agents such as atracurium or vecuronium can be used for that purpose (Jones, 1985). Atracurium in pigs, however, did not alter the pulmonary or abdominal elastic properties (Chassard *et al*, 1996); so the use of neuromuscular blocking agents during laparoscopic interventions in dogs remains controversial.

The animals should preferably be mechanically ventilated with adequate monitoring (tidal volume, inspiratory and expiratory time and positive end expiratory pressure). The minute volume has often to be increased by 20-30 % to maintain normocapnia. Whether pressure controlled or volume controlled ventilation is used, is a matter of equipment available and personal preference. Volume controlled ventilators deliver a preset tidal volume without regard for the maximum inspiratory pressure. Large tidal volumes (12-15 ml/kg) prevent alveolar atelectasis and hypoxemia, but there is a higher risk for barotrauma during intermittent positive pressure ventilation (Chui et al, 1993). Pressure controlled machines allow inspiratory volumes (depending on the compliance and airway resistance) to vary. As the anesthesiologist often has to use high airway pressure to overcome the effect of increased intra-abdominal pressure for a given volume, this method allows a more safe and efficient ventilation. Changes of respiratory compliance and increase in airway pressure during laparoscopy can be monitored using pressure-volume or flow-volume loops of a side-stream spirometry monitor. With this method, any change in airway pressure, tidal volume,

resistance or compliance can be evaluated and corrected, if needed. Postoperative analgesia is best provided with a repeated dosing of a long-acting partial mu-opioid (6-8 hours postoperative analgesia) such as buprenorphine or with an epidural analgesia.

CONCLUSION

In the future, minimally invasive surgery will surely become the method of choice for some selected surgical and diagnostic procedures (Siegl *et al*, 1994; Richter, 2001). However, both surgeon and anesthesiologist must be prepared to encounter potential problems occurring during the endoscopic intervention. The major problems are related to the cardiopulmonary effects of the pneumoperitoneum and the systemic carbon dioxide absorption. Other risks are extraperitoneal gas insufflation, venous gas embolism and unintentional injuries. Obviously a ventilator and appropriate monitoring equipment for detecting early irregularities should be available, and both surgeon and anesthesiologist should always be prepared to perform an open laparotomy.

Initially, laparoscopy takes longer to perform, but as the training and experience of the surgeon and the anesthesiologist increase, the duration of the procedure decreases.

Overall, the recently introduced technique of laparoscopy should become a so-called "safe technique", whose ultimate goal is the patient's well-being.

LITERATURE

- Bailey J.E., Pablo L.S. (1999). Anaesthetic and physiologic considerations for veterinary endosurgery. In: Freeman L.J. (editor). *Veterinary Endosurgery*. Mosby, St Louis, Missouri, USA, pp. 224-243.
- Chassard D., Berrada K., Tournadre J.P., Boulétreau P. (1996). The effects of neuromuscular block on peak airway pressure and abdominal elastance during pneumoperitoneum. *International Anaesthesia Research Society* 82, 525-527.
- Chui P.T., Gin T, Oh T.E. (1993). Anaesthesia for laparascopic general surgery. *Anaesthesia and Intensive Care* 21, 163-71.
- Duke T. (1996). Hemodynamics and respiratory function in the anesthetized patient undergoing laparascopy. In: *Proceedings 3rd International Laparoscopy Course*, Saskatchewan, Canada.
- Duke T., Steinacher S.L., Remedios A.M. (1996). Cardiopulmonary effects of using carbon dioxide for laparoscopic surgery in dogs. *Veterinary Surgery 25*, 77-82.
- Gilroy B.E.; Anson L.W. (1987). Fatal air embolism during anesthesia for laparascopy in a dog. *Journal of the American Veterinary Medical Association* 190, 552-554.

- Hall L.W., Clarke K.W., Trim C.M. (2001). Principles of sedation, analgesia and premedication. In: Hall L.W., Clarke K.W., Trim C.M. (eds). *Veterinary Anaesthesia*, Tenth Edition, W.B. Saunders, London, UK, pp 75-112.
- Iberti T.J., Kelly K.M., Gentili D.R., Hirsch S., Benjamin E. (1987). A simple technique to accurately determine intra-abdominal pressure. *Critical Care Medicine* 15, 1140-1142.
- Ivankovitch A.D., Miletich D.J., Albrecht R.F., Heyman H.J., Bonnet R.F. (1975). Cardiovascular effects of intraperitoneal insufflation of carbon dioxide and nitrous oxide in the dog. *Anesthesiology* 42, 281-287.
- Jones, R.S. (1985). New skeletal muscle relaxants in dogs and cats. *Journal of the American Veterinary Medical Association* 187, 281-282.
- Kashtan J., Green J.F., Parsons E.Q., Holcroft J.W. (1981). Hemodynamic effects of increased abdominal pressure. *Journal of Surgical Research* 30, 249-255.
- Koivusalo A.M., Lindgren L. (2000). Effects of carbon dioxide pneumoperitoneum for laparoscopic cholecystectomy. *Acta Anaesthesiologica Scandinavica 44*, 834-841.
- Kolata R.J., Freeman L.J. (1999). Access, port placement, and basic endosurgical skills. In: Freeman L.J. (editor). *Veterinary Endosurgery*. Mosby, St Louis, Missouri, USA, pp. 44-60.
- Leighton T., Pianim N., Liu S.Y., Kono M., Klein S., Bongard F. (1992). Effectors of hypercarbia during experimental pneumoperitoneum. *The American Surgeon* 58, 717-721.
- Lindberg F. (2002). Carbon Dioxide Pneumoperitoneum-Hemodynamic Consequences and Thromboembolic Complications. *Acta Universitatis Upsaliensis*.

- Martin M.F., Lima J.R., Ezquerra L.J., Carrasco M.S., Uson- Gargallo J. (2001). Prolonged anesthesia with desflurane and fentanyl in dogs during conventional and laparascopic surgery. *Journal of the American Veterinary Medical Association* 219, 941-945.
- Martin W.R. (1983). Pharmacology of opioids. *Pharmacological Reviews* 35, 283-323.
- Nolan A.M., Reid J. (1991). The use of intraoperative fentanyl in spontaneously breathing dogs undergoing orthopaedic surgery. *Journal of Veterinary Anaesthesia* 18, 30-34.
- O'Malley C., Cunningham A.J. (2001). Physiologic changes during laparascopy. *Anesthesiology. Clinics of North America* 19, 1-19.
- Richardson J.D., Trinkle J.K. (1976). Hemodynamic and respiratory alterations with increased intra-abdominal pressure. *Journal of Surgical Research* 20, 410-411.
- Richter K.P. (2001). Laparoscopy in dogs and cats. *Veterinary Clinics of North America 31* 707-727.
- Siegl H., Böhm R., Ferguson J., Friedrich M., Losert U.M. (1994). Laparoskopische Ovariohysterektomie bei einem Hund. *Wiener Tierärztliche Monatschrift 81*, 149-152.
- Williams M., Murr P.C. (1993). Laparascopic insufflation of the abdomen depresses cardiopulmonary fuction. *Surgical Endoscopy* 7, 12-16.
- Wilson D.V., Evans A.T., Carpenter R.E., Mullineaux D.R. (2004). The effect of four anesthetic protocols on the splenic size in dogs. *Veterinary Anaesthesia and Analgesia 31*, 102-108.
- Wolf J.S., Carrier S., Stoller M.L. (1994). Gas embolism: Helium is more lethal than carbon dioxide. *Journal of Laparoendoscopical Surgery 4*, 173-177.

Uit het verleden

KOEIENMEESTERS EN PAARDENMEESTERS IN DE JAREN 1600

(II)

Hoe gingen de koeienmeesters beschreven op pag. 116 volgens de gegevens te vinden in de zeventiende-eeuwse heksenprocessen te werk? Om te zien of een koe ziek was, baseerde een smid die ook koeienmeester was uit Zulte, zich louter op uiterlijke tekens, zoals de stand van de ogen van de beesten. Hij behandelde de zieke koe van Antheunis de Sloovere met aderlating en allerlei drankjes. Pieter Minne liet verstaan dat hij als koeienmeester alleen 'natuurlijke' ziekten behandelde, zoals de bloedziekte, de balgpijn, het *qualick compas* en de pest. In gevallen van 'bloedziekte' voerde hij aderlatingen uit. Uit ervaring wist hij heel goed dat de meeste koeien en paarden wormen hadden en dat die wormen bij paarden meestal in de pens (sic) en bij koeien achter het hart te vinden waren.

Als het verkeerd afliep, durfden deze 'dierenartsen' lijkschouwingen aan om op zoek te gaan naar mogelijke ziekteoorzaken. Zo sneed de paardenmeester Carel Populier het paard van Jan Minne open en vond er *fenyneghe beesten* (het Latijnse venenum of vergift betekende in de streek ook schadelijk insect) ende slym als pugereck (kikkerdril). Twee van die beesten zaten rond het hart en ze hadden elk twee vleugels. Bij de dissectie van een ander paard vond hij *fenynighe beesten* in de vorm van 'palinghen' en in koeien *fenynighe beesten ghelyck loppen* (bloedzuigers – Hirudo) ende platte ghelyck blicken (zoetwatervisje). Uit de muil van een kalf kwam er een beeste ghelyck een loppe die zich op een bord langzaam uitrok. Dat waren echter geen alledaagse bevindingen. Ze wezen op betovering ...

Bron: Monballyu J., 2003 (zie pag 116)