High intraabdominal pressure: Effects on clinical parameters and lung pathology in baboons *(Papio cynocephalus* and *Papio anubis)*

Thomas M. D'Hooghe, MD,[a] Charanjit S. Bambra, PhD,[a] Idle O. Farah, DVM,[a] Barbara M. Raeymaekers, SCM,[a] and P.R. Koninckx, MD, PhD[b]

Nairobi, Kenya, and Leuven, Belgium

OBJECTIVE: The risks of a high intraabdominal pressure during laparoscopy are poorly documented. These aspects were studied in a relevant nonhuman primate model, the baboon *(Papio anubis, Papio cynocephalus).*

STUDY DESIGN: The animals used were to be killed at the completion of a vaccine project. They were anesthetized and intubated but allowed to breathe spontaneously. In group 1 (n = 10) a fixed intraabdominal pressure (between 10 and 35 cm H_2O [7 and 26 mm Hg]) was applied over 30 minutes. In group 2 (n = 7) the intraabdominal pressure was increased up to a maximum of 105 cm H_2O (77 mm Hg). Blood vessels of the parietal peritoneum and omentum were systematically opened from 30 cm H_2O (22 mm Hg) onward. Respiration and pulse rate were measured regularly, and the degree of respiratory distress was assessed. After death of the baboons a necropsy was carried out immediately to study the degree of lung atelectasis.

RESULTS: In group 1 the respiration rate increased and the heart rate decreased. At an intraabdominal pressure of ≥30 cm H_2O (22 mm Hg) moderate respiratory distress was seen after 20 minutes. In group 2 one animal had a bilateral pneumothorax at a pressure of 60 cm H_2O (44 mm Hg) and died at 90 cm H_2O (66 mm Hg). Severe respiratory distress was observed in the other six animals. Severe lung atelectasis was present in only one of the five primates with moderate respiratory distress of group 1 and in all baboons of group 2.

CONCLUSION: An increase of intraabdominal pressure up to 105 cm H_2O (77 mm Hg) combined with intraabdominal blood vessel injury is not lethal in most baboons. (Am J Obstet Gynecol 1993;1969:1352-6.)

Key words: Baboon *(Papio anubis, Papio cynocephalus);* increase in intraabdominal pressure; blood vessel injury during laparoscopy under general anesthesia; respiratory distress; lung pathology

Although safety is of great concern in modern laparoscopy, it has not been well investigated. It has been generally accepted that the intraabdominal pressure during laparoscopy in women should not exeed 30 cm H_2O (22 mm Hg), to prevent potentially dangerous hemodynamic changes[1-3] and air embolism, especially during endoscopic surgery with damage to blood vessels. However, a further increase in intraabdominal pressure up to 40 and 54 cm H_2O (29 and 40 mm Hg) has only been studied for a period of 10 minutes and was not lethal for women,[2, 4] or for dogs,[3] although significant hemodynamic changes were observed.

Effects of an intraabdominal pressure >54 cm H_2O (40 mm Hg) cannot be studied in women because of ethical considerations. Because of their similarity to the human, baboons have been extensively used for research in cardiovascular physiology and surgery.[5] An opportunity for studying the effects of high intraabdominal pressure in this species was presented when 18 baboons had to be killed at the termination of a vaccine project.

Material and methods

Animals. The study was performed on 18 baboons (11 *Papio cynocephalus* and seven *Papio anubis*) that had to be killed at the end of a vaccine project. The primates included 14 females (11 *Papio cynocephalus* and three *Papio anubis*) and four males *(Papio anubis).* They had been maintained at the Institute of Primate Re-

From the Institute of Primate Research[a] and the Department of Obstetrics and Gynecology, University Hospital Gasthuisberg.[b]
Supported by the Commission of the European Communities (DG VIII Development and DG XII Science, Research and Development) and by the VLIR (Flemish Interuniversity Council), Brussels, Belgium.
Received for publication October 27, 1992; revised March 15, 1993; accepted July 13, 1993.
Reprint requests: T.M. D'Hooghe, MD, Department Obstetrics-Gynecology, University Hospital Gasthuisberg, B-3000 Leuven, Belgium.

0002-9378/93 $1.00 + .20 ***6/1/50051***

Table I. Clinical effects of fixed intraabdominal pressure during 30 minutes in 10 baboons undergoing laparoscopy

	Intraabdominal pressure (cm H_2O)				
	10 (n = 2)	*20 (n = 2)*	*25 (n = 1)*	*30 (n = 4)*	*35 (n = 1)*
Heart rate/respiration rate (mean)					
After 5 min	78/19	78/16	68/18	71/15	92/16
After 30 min	60/27	72/21*	68/25*	65/21†	76/36†
Heart rate/respiration rate (change)	−18/+8	−6/+5	0/+7	−6/+6	−16/+20

*Mild respiratory distress after 15 to 20 minutes.
†Moderate respiratory distress after 20 minutes.

search, Nairobi, Kenya, for 3.4 ± 2 (0.7 to 5) years. The colony management has been described previously.[6] Their weight was 12.0 ± 2.6 (6.9 to 15.7) kg.

Equipment and insufflation procedure. The equipment used for intraabdominal carbon dioxide insufflation essentially consisted of a modified water valve system.[7] The long end of a hollow metal T tube (110 cm) was inserted into a cylinder filled with water. One short end of this tube was connected with plastic tubing to a carbon dioxide cylinder while the other was connected to a 10 mm laparoscope (Storz, Tuttlingen, Germany). The intraabdominal pressure equals the insufflation pressure, which is determined only by the length of the tube under water (cm H_2O). Warming or moistening of the insufflated carbon dioxide gas was not carried out. The insufflation flow was kept <2 L/min in all the animals.

General anesthesia was induced with a mixture of 1.4 ml ketamine (10% solution, Ketaset, Aveco) and 0.6 ml thiazine hydrochloride (2% solution, Rompun, Bayer, Leverkusen, Germany) given intramuscularly. Subsequently the baboons were intubated and allowed to breathe spontaneously, inhaling a mixture of oxygen and nitrous oxide (70%/30%) and 1% halothane. The baboons were placed in a 20-degree Trendelenburg position after 10 to 15 minutes of insufflation at 10 cm H_2O (7 mm Hg). In group 1 (n = 10, all females) the intraabdominal pressure was further maintained for 30 minutes at 10 cm H_2O (7 mm Hg, n = 2), 20 cm H_2O (15 mm Hg, n = 2), 25 cm H_2O (18 mm Hg, n = 1), 30 cm H_2O (22 mg Hg, n = 4), and 35 cm H_2O (26 mm Hg, n = 1). In group 2 (n = 7, including four males) the intraabdominal pressure was increased at 10-minute intervals with increments of 5 cm H_2O (4 mm Hg, n = 1), 10 cm H_2O (7 mm Hg, n = 4), or 20 cm H_2O (15 mm Hg, n = 2). When the intraabdominal pressure had reached 30 cm H_2O (22 mm Hg), blood vessels of omentum and parietal peritoneum were cut with laparoscopy scissors and observed for the presence of gas bubbles. When a maximum intraabdominal pressure of 105 cm H_2O (77 mm Hg) was reached (n = 5), the Trendelenburg position was increased to 35 degrees for another 10 minutes. Subsequently the laparoscope was removed, allowing the intraabdominal air to escape, and the animals were immediately killed with an intravenous or intracardial injection of 8 ml of sodium pentobarbital (20% solution).

Clinical parameters. The heart rate, respiration rate, and degree of respiratory distress were recorded before and at 5-minute intervals during the laparoscopy. The heart rate was either palpated at the axillary artery or counted during laparoscopy (heart muscle contractions at the diaphragm). Respiratory distress was clinically defined as mild (superficial breathing, prolonged inspiration time, or slight tirage), moderate (pronounced tirage or nostril breathing), or severe (central cyanosis, gasping, or undetectable respiration).

Pathologic assessment. In all the animals a necropsy was performed immediately after death, and special attention was paid to the degree of lung collapse. Lung specimens for biopsy were taken at the borderline between normal and collapsed lung tissue, embedded in paraffin, cut into 7 μm sections, and stained with hematoxylin-eosin.

Ethics. This project complied with the procedure and methods outlined in the Guide for the Care and Use of Laboratory Animals of Institute of Primate Research and received the approval of the Institution Scientific Resources Evaluation and Review Committee. This committee reviews all prospective research projects with respect to the experimental design, welfare of the animals in use, management, necessity of the use of the primate model, and experience of the researchers regarding the experimental procedures required. This study was approved because useful and clinically relevant information could be obtained from animals that had to be killed at the termination of a vaccine study.

Results

Clinical parameters. Table I shows the clinical effects of a fixed intraabdominal pressure (group 1, n = 10). After the onset of insufflation the respiratory rate increased and the heart rate decreased in all animals. The

Table II. Clinical effects (heart rate/respiratory rate) of an intraabdominal pressure increase at 10-minute intervals with increments of 5, 10 or 20 cm H_2O in baboons undergoing laparoscopy (n = 7)

	Intraabdominal pressure (cm H_2O)											
	0	*15*	*30*	*40*	*50*	*60*	*70*	*80*	*90*	*100*	*105*	*105**
+5 cm (N1)	60/30	72/36	56/20†	50/8‡	52/3	80/28§	86/40	120/38‖	–	–	–	–
+10 cm												
N2, 3, 4¶	83/26	84/21	85/23†	83/21	73/23	77/22§	75/23‡	75/22	84/23§	83/21	94/21	105/20
N5	80/20	66/20	62/18	60/24†	60/22§	52/22	??/25‡	47/05	00/00	–	–	–
+20 cm (N6, 7)¶	80/19	63/16	64/19	–†	57/22#	–‡	49/24#	–	54/24#	–	67/28#	66/28#

*Trendelenburg position increased from 20 to 35 degrees.
†Onset of mild respiratory distress.
‡Onset of severe respiratory distress.
§Onset of moderate respiratory distress.
‖No intraabdominal pressure increase beyond 85 cm H_2O (leakage of water column).
¶Mean values for heart rate/respiratory rate.
#Respiratory rate of N7 only (not detectable in N6).

five primates with an intraabdominal pressure of ≥30 cm H_2O (22 mm Hg) showed moderate respiratory distress after 20 minutes. All the baboons of this group survived the procedure.

Table II shows considerable interindividual variation in the clinical effects of a stepwise increase in intraabdominal pressure (group 2, n = 7). All animals had mild respiratory distress at 30 cm H_2O (22 mm Hg). The onset of severe respiratory distress at 40 cm H_2O (29 mm Hg, n = 1), 60 cm H_2O (44 mm Hg, n = 1), or 70 cm H_2O (51 mm Hg) was usually associated with a drop in heart rate, followed by a rise (n = 6). One baboon (N5) developed a bilateral pneumothorax at 60 cm H_2O (44 mm Hg), followed by a drop in heart rate and respiratory rate, subcutaneous emphysema of head and upper limbs at 80 cm H_2O (59 mm Hg), and death at 90 cm H_2O (66 mm Hg). When intraabdominal pressure was increased with 20 cm H_2O (15 mm Hg) each for 10 minutes one animal (N6) had undetectable respiration at 50 cm H_2O (40 mm Hg), followed by a drop in heart rate and facial edema at 90 cm H_2O (66 mm Hg). The other (N7) showed occasional gasping from 70 cm H_2O (51 mm Hg) onward.

Opening of the blood vessels of omentum and parietal peritoneum resulted in variable degrees of intraabdominal bleeding and blood clot formation, but clear gas bubbles were not observed. Electrocoagulation of the cut vessel was never required because the bleeding always stopped spontaneously soon after injury, especially at high intraabdominal pressure.

Pathologic studies. The atelectatic areas of the lung were generally collapsed, dark blue (widespread hemorrhage), and subcrepitant. These areas also appeared shrunken, depressed, and well demarcated from the rest of the lung tissue, especially when compensatory emphysema was present. According to the degree of atelectasis the animals were classified in three different groups: mild, moderate, and severe lung collapse (Table III). A good correlation was found between the degree of respiratory distress and lung collapse. Severe lung collapse was present in eight baboons, including all the primates with severe respiratory distress (n = 7) and one animal with moderate respiratory distress. In six of these eight baboons atelectasis was found in the posterior lung lobes where respiratory excursions are deep. The lung lobes of the baboon (N5) that died after bilateral pneumothorax appeared liver-like and sank in a 10% formalin solution, indicating complete collapse. Microscopic examination confirmed complete atelectasis without compensatory emphysema. Severe congestion and multifocal intraalveolar hemorrhage were present. Blood vessels and bronchioles appeared compressed. Pulmonary edema was present in four animals, including three with severe respiratory distress. Congestion and friability was found in the other visceral organs, and it correlated well with the level of intraabdominal pressure used. Obvious gas bubbles in the cardiovascular system were not observed, and the blood did not have a frothy appearance. No macroscopic or microscopic alveolar collapse was evident in the one baboon that was killed after induction of anesthesia and without subsequent intraabdominal carbon dioxide insufflation.

Comment

From the results presented above it is obvious that an increased respiratory rate and a decreased heart rate were observed when a fixed intraabdominal pressure (between 10 and 35 cm H_2O, or 7 and 26 mm Hg) was used. The increased respiratory rate can be considered as a compensatory phenomenon for the reduction in lung expansion and has also been noted in patients with epidural anesthesia[8] undergoing laparoscopy with an intraabdominal pressure up to 34 cm H_2O (25 mm

Table III. Pathologic classification of lung collapse

	Macroscopic	*Microscopic*
Mild	Peripheral collapse of at least one lung lobe	Few areas of atelectasis; rest of lung tissue appears normal
Moderate	Complete collapse of at most one lung lobe with peripheral collapse of the other lobes; normal areas still present	Considerable atelectasis with congestion; a few areas with hemorrhage or emphysema
Severe	Complete collapse of at least two lung lobes with peripheral collapse of the other lobes	Massive atelectasis, widespread congestion, hemorrhage, compensatory emphysema

Hg). The relative bradycardia observed could be a consequence of reflex vagal stimulation from stretching or distention of the peritoneum.[9] A mild decrease in heart rate has also been reported in both spontaneously breathing and artificially ventilated patients when a laparoscopy was performed at an intraabdominal pressure up to 34 cm H_2O (25 mm Hg).[10] However, most investigators found a stimulation of the cardiovascular system (tachycardia, increased central venous pressure, mild hypertension) in the same patient population at an intraabdominal pressure <27 cm H_2O (20 mm Hg).[1, 2, 4, 11, 12] The hemodynamic effects of a further intraabdominal pressure increase from 27 to 40 or 56 cm H_2O (from 20 to 29 or 41 mm Hg) were observed only for 10 minutes in women[2, 4] and dogs,[3] respectively. In both studies tachycardia and a decreased cardiac output were found, suggesting diminished venous return. Normal values were measured shortly after the release of the IAP. Similarly, in the current study tachycardia was observed in baboons that coped with or recovered from severe respiratory distress. However, the reversibility described in the studies mentioned above[2-4] cannot be extrapolated to our study because a high intraabdominal pressure was maintained during only 10 minutes compared with 30 minutes in the baboons. Furthermore, both women and dogs were artificially ventilated and baboons were not.

In this study on baboons the degree of respiratory distress was defined according to clinical criteria only, because facilities for taking an electrocardiogram or measuring blood pressure, central venous pressure, lung function, blood gases, and pH were not available. Only mild respiratory distress was found if the intraabdominal pressure was <30 cm H_2O (22 mm Hg) for 30 minutes. Similarly, no major respiratory or hemodynamic dysfunction has been reported in spontaneously breathing women during laparoscopies performed at an intraabdominal pressure <34 cm H_2O (25 mm Hg) during a maximum of 15 minutes.[10, 13] Furthermore, it is worth noting that baboons recovered without any problems after laparoscopy at an intraabdominal pressure up to 15 cm H_2O (11 mm Hg) during 90 minutes.[14] However, the reversibility of the severe respiratory distress noted in the current study cannot be addressed because, for ethical reasons, the animals were killed immediately after release of the pneumoperitoneum. Reversibility would depend on the degree and consequences of central hypoxia and on the reversibility of lung collapse. Atelectasis is known to be reversible as soon as the causative agent is removed.[15, 16] The atelectasis resulting from abdominal distension is usually partial, typically affecting the anterior lung segments where respiratory excursions are shallow. However, collapse of the posterior lung lobes, where respiratory excursions are deep, was noted in six of the seven cases of severe lung collapse in this study. It is known that extensive atelectasis produces severe respiratory difficulties, and if bilateral it can result in death.[15] Severe (acute) bloat in cattle[17] and gastric dilatation in nonhuman primates[18] have been shown to be fatal, primarily because of the resulting respiratory embarrassment.

It is remarkable that only one baboon died, taking into account the high intraabdominal pressure and the intraabdominal bleeding in the second group. Bilateral pneumothorax associated with pneumoperitoneum has been described before[19, 20] and is considered to be a rare complication of laparoscopy. This could have resulted either directly from the high intraabdominal pressure leading to diaphragmatic and pleural rupture or indirectly from subperitoneal air extension to both pleurae with secondary rupture.[19]

Carbon dioxide embolism is considered another rare complication of laparoscopy. However, criteria for diagnosis of this condition vary considerably in the literature, and this explains why data on prevalence are difficult to obtain.[21] Methods for diagnosing venous air embolism include auscultation for characteristic "mill wheel" murmurs, placement of a Doppler flow detector over a specific area on the thoracic wall and measuring end-tidal carbon dioxide concentrations.[22] However, it seems that the only absolute criterion for diagnosis of gas embolism is the confirmation of gas bubbles in the vascular system at the time of surgery or autopsy.[21] Opening of the heart and major pulmonary trunks under water to detect the escaping gas has been reported to be a good test.[14] This was not done in the current study, but obvious gas bubbles were not ob-

served in the vascular system either during surgery or at necropsy. These data suggest that major air embolism did not occur, although a high intraabdominal pressure was used and intraabdominal blood vessels were opened. Because bleeding usually stopped soon after the vessels were opened, it is possible that these were sealed by the high intraabdominal pressure and that the surface through which carbon dioxide could enter the circulation was limited. In other publications[23] it has been suggested that increased intraabdominal pressure might lead to vein rupture, allowing carbon dioxide to enter the circulation. This hypothesis was not confirmed in this study; no significant intraabdominal bleeding was observed from other sources than the injured vessels.

In conclusion, this study presents the first experimental evidence that an increase of intraabdominal pressure, at least up to 105 cm H_2O (77 mm Hg), is not lethal in the majority of anesthetized but spontaneously breathing baboons, even after intraabdominal blood vessel injury. However, one animal died as a consequence of bilateral pneumothorax, and severe effects on clinical parameters and lung pathologic conditions were observed in the other primates.

We thank Prof. Dr. E. Vandermeersch (Department of Anesthesiology) and Prof. Dr. J. Lauweryns (Department of Pathology) from the University Hospitals Gasthuisberg and St.-Rafael, Leuven, Belgium, for interpreting the data of this study. We also thank the collaborating centers: Maurice Bruhat, MD, Clermont-Ferrand, France; Joaquin Calaf, MD, Barcelona, Spain; Hans Evers, MD, PhD, Maastricht, The Netherlands; Jef Raus, MD, PhD, Diepenbeek, Belgium; and Marc Dhont, MD, PhD, Gent, Belgium. The help of advisors Arthur F. Haney, MD, Duke University, Durham, North Carolina; Robert S. Schenken, MD, San Antonio, Texas, and Daniel C. Martin, MD, PhD, Memphis, Tennessee, is greatly appreciated. We also thank Zakariah M. Karanja and Sammy Kisara for the indispensible clinical assistance. Furthermore, we highly appreciate the histologic processing of lung biopsies by Mr. Peter S.N. Machai and Mr. Richard K. Korir. We thank Mrs. Storz-Rehling (Storz Company, D-7200 Tuttlingen, Germany) for the generous supply of the endoscopy equipment, and the support of Dr. Lempereur (Ipsen NV, Belgium) is appreciated. The VVOB (Flemish Association for Development Cooperation and Technical Assistance) provided administrative support for this study.

REFERENCES

1. Hodgson C, McClelland RMA, Newton JR. Some effects of the peritoneal insufflation of carbon dioxide at laparoscopy. Anaesthesia 1970;25:382-90.
2. Kelman GR, Swapp GH, Smith I, Benzie RJ, Gordon NLM. Cardiac output and arterial blood-gas tension during laparoscopy. Br J Anaesth 1972;44:1155-61.
3. Ivankovich AD, Miletich DJ, Albrecht RF, Heyman HJ, Bonnet RF. Cardiovascular effects of intraperitoneal insufflation with carbon dioxide and nitrous oxide in the dog. Anesthesiology 1975;42:281-7.
4. Motew M, Ivankovich AD, Bieniarz J, et al. Cardiovascular effects and acid-base and blood gas changes during laparoscopy. Am J Obstet Gynecol 1973;115:1002-11.
5. Fridman EP, Popova VN. Species of the genus *Papio (cercopithecidae, primates)* as subjects of biomedical research. II. Quantitative characteristics of contemporary use of baboon species in medical and biological investigations. J Med Primatol 1988;17:309-18.
6. Else JG, Tarara R, Suleiman MA, Eley RM. I. Enclosure design and reproductive success of baboons used for reproductive research in Kenya. Lab Anim Sci 1986;36: 168-72.
7. Koninckx PR, Vandermeersch E. The persufflator: an insufflation device for laparoscopy and especially for CO_2-laser-endoscopic surgery. Hum Reprod 1991;6:1288-90.
8. Ciofolo MJ, Clergue F, Seebacher J, Lefebvre G, Viars P. Ventilatory effects of laparoscopy under epidural anesthesia. Anesth Analg 1990;70:357-61.
9. Carmichael DE. Laparoscopy—cardiac considerations. Fertil Steril 1971;22:69-70.
10. Harris MNE, Plantevin OM, Crowther A. Cardiac arrhythmias during anesthesia for laparoscopy. Br J Anaesth 1984;56:1213-6.
11. Smith I, Benzie RJ, Gordon NLM, Kelman GR, Swapp GH. Cardiovascular effects of peritoneal insufflation of carbon dioxide for laparoscopy. BMJ 1971;3:410-1.
12. Marshall RL, Jebson PJR, Davie IT, Scott DB. Circulatory effects of carbon dioxide insufflation of the peritoneal cavity for laparoscopy. Br J Anaesth 1972;44:680-4.
13. Kurer FL, Welch DB. Gynaecological laparoscopy: clinical experiences of two anaesthetic techniques. Br J Anaesth 1984;56:1207-12.
14. D'Hooghe TM, Bambra CS, Cornillie FJ, Isahakia M, Koninckx PR. Prevalence and laparoscopic appearance of spontaneous endometriosis in the baboon *(Papio anubis, Papio cynocephalus)*. Biol Reprod 1991;45:411-6.
15. Cotran RS, Kumar V, Robbins SL. The respiratory system. In: Cotran RS, Kumar V, Robbins SL, eds. Pathologic basis of disease. 4th ed. Philadelphia: WB Saunders, 1989: 758-9.
16. Jubb KVF, Kennedy PC, Palmer N. The respiratory system. In: Jubb KVF, Kennedy PC, Palmer N, eds. Pathology of domestic animals, vol 2. 3rd ed. San Diego: Academic Press, 1985:442-3.
17. Blood DC, Radiostits OM, Henderson JA. Diseases of the alimentary tract. II. In: Blood DC, Radiostits OM, Henderson JA, eds. Veterinary medicine. 6th ed. Eastbourne, England: English Language Book Society and Balliere-Tindall, 1983:239-46.
18. Pond CL, Newcomer CE, Anver MR. Acute gastric dilatation in nonhuman primates. Review and case studies. Vet Pathol 1982;19(suppl 7):126-33.
19. Ronsse G, Stalport J, Burnon D. Pneumothorax bilateral, complication exceptionnelle d'une laparoscopie gynecologique. Acta Chir Belg 1980;5:345-8.
20. Shapiro M. Spontaneous pneumothorax complicating pneumoperitoneum therapy. A review and report of a case. Ann Intern Med 1955;43:876-92.
21. Yacoub OF, Cardona I, Coveler LA, Dodson MG. Carbon dioxide embolism during laparoscopy. Anesthesiology 1982;57:533-5.
22. Gilroy BA, Anson LW. Fatal air embolism during anesthesia for laparoscopy in a dog. J Am Vet Med Assoc 1987; 190:552-4.
23. McKenzie R. Laparoscopy. N Z Med J 1971;74:87-91.