# 2 Physiology of Pediatric Genitourinary Laparoscopy

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**Abstract** The expanding scope of paediatric genitourinary laparoscopy has meant that increasingly complex procedures are being carried out in ever younger patient populations. Surgeons and anaesthetists alike have thereby been confronted with and gained awareness of a mounting repertoire of physiological consequences related to both intra and retroperitoneal gaseous insufflation. The physiological responses encountered clinically are mainly due to the mechanical and biochemical effects of carbon dioxide ($CO_2$) insufflation. $CO_2$ is absorbed across the thin peritoneal membrane of paediatric patients resulting in hypercarbia and acidosis and leads to an increased $CO_2$ load presented to the lungs. Mechanically, the increased intraabdominal pressure decreases lung compliance and worsens ventilation perfusion mismatch, ultimately leading to hypoxia. Cardiovascularly, the paediatric patient is prone to developing increases in systemic and pulmonary vascular resistance resulting in significant decreases in cardiac output. These cardiopulmonary effects are pressure dependent and have an occurrence that is inversely proportional to patient age and weight, warranting use of the lowest insufflation pressures possible, especially when dealing with very young and/or acutely ill patients.

Abdominal insufflation also leads to acute elevations in intracranial pressure, a caveat with specific relevance to genitourinary laparoscopy as myelodysplastic patients constitute a significant patient subgroup who stand to benefit from laparoscopic procedures under specific precautionary measures. Other physiological consequences include effects on renal function, thermoregulation, surgical stress and metabolism. Despite this long list of untoward physiological effects the overwhelming majority of genitourinary

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laparoscopic procedures in paediatric patients are carried out safely as long as proper close monitoring, and required ventilatory adjustments are instituted.

**Keywords** Physiology · Insufflation · Laparoscopy · Robotics · Paediatrics

## 1. INTRODUCTION

Safe and successful laparoscopic surgery is dependent on the creation of sufficient working space in the abdominal cavity, to allow adequate visualization and enough room for manipulation of laparoscopic instruments. This is even more of an issue when it comes to laparoscopy in children and infants, let alone the neonates, who by the very nature of their tiny and compact anatomy rarely allow more than a few centimetres of vertical working space under the best of conditions *(1)*. To achieve these ends, various methods and contraptions have been employed of which creation of pneumoperitoneum (PnP) is by far the most prevalent *(2,3)*. PnP facilitates laparoscopy by expanding the abdominal cavity and suppressing the bowels and viscera thereby giving the laparoscopic surgeon overview and unhindered manoeuvrability. However for all its advantages, PnP brings with it a whole host of "if not unforeseen" then at least to some extent "often neglected" physiological ramifications which surgeons and anaesthetists have only slowly but steadily begun to identify and appreciate.

In paediatric urology, as in other specialities, where indications for laparoscopy have been expanding exponentially it is only natural that physiological aspects of minimally invasive surgery are receiving increasing attention. Especially as technological advances, miniaturization of instruments and the introduction of robotics have meant that increasingly complex procedures are being carried out in an ever younger patient population. Furthermore, genitourinary minimally invasive surgery, in light of its specifics, entails that some procedures can be performed via retroperitoneoscopic access which adds yet another dimension to the understanding of percutaneous endoscopic surgical physiology. The current chapter explores the physiology of genitourinary laparoscopy based on evidence acquired from a growing body of literature, and will try to present hitherto agreed upon facts in a clinical context and as they pertain to paediatric urology.

## 2. ABDOMINAL INSUFFLATION

In genitourinary minimally invasive surgery, access can be attained by either the transperitoneal or retroperitoneal route. Initial access in both instances is achieved by open cut down techniques *(4,5)* A trocar is subsequently introduced through which gas is insufflated at variable rates to achieve pressures that range between 6 and 15 mmHg. The ideal insufflant has yet to be identified, and in its absence carbon dioxide ($CO_2$) has been found to be the most suitable alternative. The "ideal" gas would have to have limited absorption and no physiological effects when absorbed. Furthermore, it would have to have a high solubility in blood and be rapidly excreted if absorbed or inadvertently injected intravascularly so as to limit any possibility of air embolus formation. Last and in no way least such a gas should not be capable of supporting combustion. Air and oxygen have limited physiological systemic effects but cannot be considered as they support combustion. Helium, which is an inert gas, has minimal systemic effects; however, it is relatively insoluble thereby increasing the risks of air embolism and cardiovascular complications during laparoscopy *(6,7)*. It has however been used successfully in selected adult patients deemed unfit for $CO_2$ PnP due to severe cardiovascular compromise and inability of effective $CO_2$ clearing *(8)*. Other gases such as nitrous oxide, nitrogen and argon have also been evaluated but never achieved widespread use as their drawbacks exceed any potential advantage over $CO_2$ (Table 1) *(9)*. $CO_2$ is thus the gas of choice at the vast majority of laparoscopic centres; it is colourless, odourless and cheap, has a high solubility in blood and is readily excreted by the lungs once absorbed. $CO_2$ is however readily absorbed leading to hypercarbia and acidosis with the potential for attendant deleterious systemic effects.

**Table 1**
**Different insufflants and their characteristics**

| *Gas* | *Blood solubility* | *Systemic effects* | *Combustion* | *Comment* |
|---|---|---|---|---|
| "Ideal gas" | High | None | Suppresses combustion | Ideal, no disadvantages fulfils all criteria. Non existent! |
| Carbon dioxide | High | Yes | Suppresses combustion | Substantial transperitoneal absorption leading to systemic side effects, and peritoneal irritation. However, low risk of gas emboli |
| Helium | Low | Minimal | Suppresses combustion | Risk of gas embolism |
| Nitrous oxide | Low | Minimal | Supports combustion under certain circumstances | Risk of gas embolism. May have analgesic effects |

(*Continued*)

**Table 1**
**(Continued)**

| *Gas* | *Blood solubility* | *Systemic effects* | *Combustion* | *Comment* |
|---|---|---|---|---|
| Atmospheric air | Low | Minimal | Supports combustion | Supports combustion, and there is substantial risk of air emboli |
| Nitrogen | Low | Minimal | Suppresses combustion | Risk of gas embolism |
| Argon | Low | Minimal | Suppresses combustion | Risk of gas embolism |

## 3. PULMONARY RESPONSE

Intra and retroperitoneal $CO_2$ insufflation lead to abdominal distension and an increase in intraabdominal pressure (IAP). The diaphragm is pushed in a cephalad direction and its excursion is limited by the increased IAP. This leads to a decrease in total lung compliance, an increase in peak inspiratory pressure (PIP) and a decrease in functional residual capacity (FRC) relative to closing pressure. These changes further increase the ventilation perfusion mismatch which already is skewed by the effects of general anaesthesia and mechanical ventilation. Combined with the absorption of $CO_2$ occurring across the stretched peritoneum, this may lead to hypercarbia, acidosis and ultimately hypoxemia especially in neonates and infants who have a low FRC, high closing pressure and high oxygen consumption. Patient positioning in the head down Trendelenburg position, as is often required in genitourinary laparoscopy, may further aggravate matters.

$CO_2$ absorption from the intra or retroperitoneal spaces leads to an increased load of $CO_2$ to the lungs, with an increased elimination *(10–12)* and can lead to acid-base imbalances in the form of acidosis *(13–16)*. Studies in paediatric patients have consistently documented significant increases in end tidal $CO_2$ (ET $CO_2$) in response to $CO_2$ insufflation *(1,10,17–23)*. In a retrospective institutional review of neonatal laparoscopy, Kalfa et al. found that ET $CO_2$ increased with an average of 33% over basal value in the majority of their patients despite ventilatory adjustments. This was higher than what is generally observed in adults, and overall these changes warranted adjustment of ventilatory minute volume to counteract the effects of the building hypercarbia in 84% of their cases. Furthermore, they were able to correlate the rise in ET $CO_2$ to insufflation pressure and length of procedure. An IAP $<6$ mmHg and procedures of shorter duration were thus less likely to be associated with ET $CO_2$ spikes *(18)*. A similar correlation between insufflation pressure and ET $CO_2$ was reported by Bannister et al. who examined the effects of stepwise increase in insufflation pressure on several cardiorespiratory parameters of infants less than 12 months old. On average ET $CO_2$ increased by 13% and 41% of the patients developed some degree of hypoxemia, rendering at least one ventilatory adjustment necessary in 95% of their patients to restore ET $CO_2$ to within 10% of baseline value. The cut-off IAP at which changes in ET $CO_2$ and other parameters occurred was 10 mmHg *(17)*.

$ETCO_2$ is clinically used as a surrogate measure for arterial $CO_2$ partial pressure ($PaCO_2$) and plays an important role in anaesthetic monitoring *(12)*. There is however some debate as to whether ET $CO_2$ accurately reflects $PaCO_2$ especially in ventilated children undergoing laparoscopic surgery where ET $CO_2$ may misestimate $PaCO_2$ in the setting of increasing alveolar dead space and worsening of ventilation–perfusion mismatch. It is therefore recommended that monitoring be supplemented by arterial blood gas analysis especially during longer laparoscopic procedures *(19)*. Based on non-invasive ET $CO_2$ monitoring however, it has been shown that a 30–40% increase in minute volume ventilation is needed in order to maintain ET $CO_2$ in children undergoing laparoscopy *(20)*. A more reliable method of assessing $CO_2$ absorbed is by metabolic monitoring whereby the total amount of $CO_2$ eliminated from the lungs is measured (VE $CO_2$). This total amount of eliminated $CO_2$ represents both the $CO_2$ produced by metabolism and that absorbed. Simultaneous measurement of oxygen consumption indicates how much of the change in pulmonary $CO_2$ is the result of pure absorption *(11)*. In adult patients undergoing therapeutic laparoscopy, metabolic monitoring showed a significant build up of $CO_2$ absorption which plateaued within 15–30 minutes after institution of PnP and that VE $CO_2$ returned to baseline within 10 minutes of exsufflation *(11,12)*. Contrary to these findings and using a similar method, McHoney and colleagues studied VE $CO_2$ in paediatric patients undergoing laparoscopy comparing them to an age matched group who had open surgery *(10)*. This study also revealed a significant increase in VE $CO_2$ in children undergoing laparoscopic surgery; however, no plateau was reached indicating a continuous absorption of $CO_2$ across the peritoneal membrane throughout the duration of the procedure. The authors speculated that this might be a reflection of a different handling of intraperitoneal $CO_2$ in children as compared to adults and may be related to the characteristics of the thin peritoneal membrane in younger age groups which may allow more $CO_2$ absorption and a longer time before steady state is achieved. Furthermore, they noted a significant inverse correlation between VE $CO_2$ and patient age and weight which again adds credence to the aforementioned premise. A similar inverse relationship between age and $CO_2$ absorption was reported by Hsing *(24)*. Comparisons between intra and retroperitoneal $CO_2$ absorption are inconclusive. In pigs no significant difference in absorption was noted while a canine study showed that intraperitoneal insufflation lead to a more pronounced rise in $PaCO_2$ *(25,26)*. Adult human studies indicate that significantly more $CO_2$ is absorbed during retroperitoneal insufflation and that this might be related to a continued dissection of the retroperitoneal space which increases the surface area in contact with $CO_2$.

Retroperitoneoscopy has also been associated with higher risks of developing surgical emphysema and pneumomediastinum *(11,12,27)*. In children no direct comparisons between the two insufflation routes have been published.

There is a time lag for ET $CO_2$ to return to normal after exsufflation of the peritoneal cavity. Studies have shown this time frame to vary between 5 and 10 minutes depending on patient age and the accumulated amount of $CO_2$ and its effective washout by ventilatory adjustment performed during surgery *(23,24)*. In 35% of their patients McHoney et al. recorded an actual brisk rise in VE $CO_2$ upon exsufflation which peaked at about 6 minutes post exsufflation and lasted for an average of 17 minutes. This unexpected phenomenon was attributed to the systemic redistribution of $CO_2$-rich blood after relief of the tamponade effect of PnP on the venous return from the lower limbs, or the sudden increase in minute ventilation as IAP rapidly normalized upon exsufflation *(10)*. This time lag in normalization of both ET $CO_2$ and VE $CO_2$ is a sign of a persistent $CO_2$-burden post exsufflation, which is handled by respiratory excretion. Clinically, this warrants continued close monitoring of especially younger children in the immediate postoperative period.

Mechanical effects of PnP and patient positioning have also been examined and have been found to contribute significantly to any respiratory impairment observed. The infant is a diaphragmatic breather and hence the cephalad diaphragmatic shift caused by increased IAP and the Trendelenburg position impairs the infant's respiratory capabilities and renders them dependant on mechanical ventilation. In its self, the Trendelenburg position decreased lung compliance by 17%, and increased PIP by 19%. Addition of 12 mmHg PnP further decreased compliance by 27% compared to baseline and increased PIP by 32% of baseline value *(22)*. Decreases in lung compliance of up to 50% have also been reported in infants less than 12 months of age utilizing insufflation pressures between 12 and 15 mmHg *(17)*. Furthermore, increased IAP significantly decreases tidal volume (17) and so in combination these derangements in ventilatory parameters may have serious consequences especially as paediatric ventilators are pressure cycled, and thus careful monitoring is warranted in order to prevent hypoventilation and hypoxemia which is not an infrequent occurrence as assessed by non-invasive monitoring using pulse oximetry. Hypoxemia is usually mild to moderate even in neonates and can be easily corrected by increasing minute ventilation and using positive end expiratory pressure *(1,17,18)*. It is worth noting that sudden onset of hypoxemia in patients undergoing renal procedures may indicate development of pneumothorax. This complication, although rare, has been reported in paediatric patients, developing as a result of direct injury to the pleura in relation to trocar placement and dissection, or may in this patient group be the result of gas moving through unrecognized congenital defects between the peritoneum and pleura such as diaphragmatic defects or pleuroperitoneal fistulas *(28–30)*. In adults risk factors for developing pneumothorax include operative durations of above 200 minutes, retroperitoneoscopic approach and an ET $CO_2$ >50 mmHg *(27,31)*.

Despite the detrimental effects of laparoscopy on pulmonary function, an overwhelming majority of clinical studies have found laparoscopy in the paediatric age group to be safe. Overall, laparoscopy even seems to confer respiratory benefits in terms of improved rates of extubation, shorter recovery room stays and shorter durations of chest physiotherapy when compared to open surgery *(32)*. So pulmonary changes that, in absolute terms significantly worsen with laparoscopy seem to have minimal clinical impact as long as proper anaesthetic monitoring is maintainedThis also holds true for neonates in whom on table extubation was possible in 60% of patients in one study *(1,18)*.

## 4. CARDIOVASCULAR RESPONSE

As there is close relationship between the cardiovascular and pulmonary systems, it is no surprise that the effects of abdominal insufflation are to be felt here. The cardiovascular response to increased IAP can be complex and depends on a multitude of factors such as preload, systemic vascular resistance, myocardial contractility and their interplay with different levels of IAP and patient position. Furthermore, hypercarbia may influence the cardiovascular system indirectly via activation of neurohormonal pathways. Therefore the resultant cardiovascular effect depends on the prevailing circumstances and cannot always be predicted in advance. In adult studies increased IAP leads to increases in systemic and pulmonary vascular resistance in addition to increases in mean arterial pressure. Heart rate remains largely unaffected by PnP whereas cardiac output decreases by up to 30% *(33,34)*. Similar outcomes have been reported in different paediatric age groups albeit with some deviations. In 6–30 month old boys undergoing laparoscopy for non-palpable testes at an IAP of 10 mmHg and in the horizontal position, Gueugniaud et al. using ultrasonic flow measurements reported a 30% decrease in cardiac output and significant decrease in stroke volume combined with an increase in systemic vascular resistance whereas blood pressure remained stable *(35)*. Similarly, in studies by Sakka et al. and Kardos et al. using slightly higher insufflation pressures of 12 mmHg, cardiac index (cardiac output indexed to body surface area) decreased 13% and 25% respectively, and there was in both studies concomitant increases in mean arterial blood pressure and systemic vascular resistance. Heart rate and stroke volume showed decreasing trends *(36,37)*. In the study by Sakka et al. IAP was lowered to 6 mmHg which resulted in normalization of the cardiac index and other cardiovascular parameters. Curiously, raising the pressure again to 12 mmHg did not alter the cardiac index as it initially had done *(36)*. Low pressure PnP of 5 mmHg in patients under 3 years of age has even been associated with a 22% increase in cardiac index, and significant increases in heart rate and mean arterial pressure *(16)*. These apparently conflicting results could be the result of different study designs and anaesthetic protocols. Patient positioning differed in the aforementioned studies in that patients were in the supine position in the studies that showed decreased cardiac output whereas they were in the reverse Trendelenburg position in the study by De Waal that showed increased cardiac output. Another plausible explanation to the observed differences could be related to the different IAP used. It has been put forward that abdominal insufflation to pressures less than that of the right atrium leads to the squeezing of blood out of the venous capacitance vessels in the splanchnic circulation leading to an increase in venous return and thereby an increase in cardiac output. Insufflation pressures exceeding those of the right atrium would on the other hand lead to compression of the vena cava whereby preload decreases and which consequently translate into a decreased cardiac output. Additional increases in IAP would lead to compression of the aorta and splanchnic vessels hence increasing cardiac afterload which also would lead to further decreases in cardiac output *(16)*. Intravascular volume depletion is therefore to be avoided as it decreases preload and in combination with vascular compression caused by PnP may lead to a higher risk of cardiovascular collapse in dehydrated patients. In neonates and infants with congenital heart disease, use of excessive IAP may even lead to temporary or permanent reopening of intracardial shunts (foramen ovale or ductus arteriosus) increasing the risk of air embolism and heart failure *(16,38)*. Such occurrences have even been reported in adults undergoing laparoscopy *(39)*.

Other than its mechanical effects PnP most likely also affects the cardiovascular system indirectly by activating different neurohormonal pathways. Animal and adults studies show that PnP results in progressive and significant increases in plasma concentrations of cortisol, epinephrine, norepinephrine, renin, and vasopressin. Changes in vasopressin plasma concentrations closely paralleled the increases in systemic vascular resistance and seemed to be related to $CO_2$ absorption as Argon insufflation did not lead to a similar response. Administration of clonidine which is a known inhibitor of vasopressin release partially blunted this response *(33,40)*. Studies in paediatric age groups are lacking however similar mechanisms seem very plausible in children.

Based on the aforementioned studies an IAP of 6 mmHg in neonates and infants has emerged as the safe level at which cardiovascular derangements are avoided. It is however again to be noted that cardiovascular effects of PnP which in absolute terms may seem significant appear to have minimal clinical impact so long as infants are appropriately monitored as witnessed by a number of studies that have employed even higher levels of IAP and have reported stable cardiovascular parameters and no occurrences of hypotension *(17,35,41)*. There have even been reports of infants with congenital heart disease successfully undergoing laparoscopy at pressures of 12 mmHg *(42,43)*. The 6 mmHg level is therefore not intended as an absolute cut-off, but serves rather as a guideline.

## 5. RENAL RESPONSE

As postnatal renal function continues to evolve throughout childhood, benefits from laparoscopy would have to be weighed against any potential harm afflicted on the developing kidneys *(44)*. Studies concerning renal function in children undergoing laparoscopy are however lacking. Existing evidence stems from animal and adult studies and will therefore have to be cautiously extrapolated to the paediatric patient. Human studies and various animal models have consistently shown that PnP affects renal function. In a recent review of all relevant literature on this subject, Demyttenaere et al. found compelling evidence of a decrease in renal blood flow during PnP. This decrease was pressure dependent and was found to worsen with certain patient positioning such as the reverse Trendelenburg position. Furthermore it was noted that adequate hydration mitigated this decrease and that the type of insufflant was irrelevant. Looking at renal function and urine output the same paper detailed consistent evidence supporting a decrease in glomerular filtration rate and urine output during PnP. In both instances the changes were seen to be temporary normalizing upon exsufflation and of unclear clinical significance. It is however most likely that such changes were of no significant implication for healthy individuals *(45)*.

In a lone study elucidating the effects of PnP on urine output in children aged 7 days to 15 years, Gómez Dammeier et al. showed that an IAP of 8 mmHg resulted in anuria within 45 minutes of establishing PnP in 88% and 14% of children under and over one year of age respectively. Furthermore, 41% of the children older than 1 year became oliguric. Postoperatively, urine output increased significantly in a compensatory manner peaking at 5 hours post exsufflation *(46)*. Mechanisms underlying this transient dysfunction are most likely multifactorial and could be related to the mechanical effects of raised IAP which may directly compress the renal cortex and or the renal veins, in combination with the previously mentioned cardiovascular effects that ultimately lead to a decrease in cardiac output and stimulation of neurohormonal vasoactive pathways which in due course lead to decreased renal perfusion, and a fall in glomerular filtration rate and diuresis *(47,48)*. Again as in the adult population, the clinical relevance of these findings is unclear. In practice this should be kept in mind when calculating intravenous fluid requirements during surgery as urine output under these circumstances cannot be considered an accurate metric. Nevertheless, judging by practical evidence, healthy children seem to weather this transient renal impairment. Studies in children with impaired renal function are lacking and patently needed.

## 6. NEUROLOGICAL RESPONSE

The effects of PnP on the central nervous system have been thoroughly described in various animal studies. Creation of $CO_2$ PnP leads to prompt and sustained elevations in intracranial (ICP) pressure that normalize upon exsufflation. Mechanisms underlying this increase include the mechanical effects of increased IAP which shifts the diaphragm in a cephalad direction narrowing the inferior vena cava and elevating intrathoracic pressure. This in turn leads to intracranial venous stasis and a decreased resorption of cerebrospinal fluid in addition to impaired drainage of cerebrospinal fluid at the level of the lumbar venous plexus. The increases in ICP are directly proportional to the level of IAP. Biochemically, the absorbed $CO_2$ which leads to varying degrees of hypercarbia induces cerebral arteriolar vasodilatation which further increases ICP. Trendelenburg position and hypoventilation also significantly increase ICP whereas diametric manoeuvres, i.e. reverse Trendelenburg and hyperventilation, only partially restore normalcy *(49–53)*. Using infrared spectroscopy De Waal and co-workers were able to show considerable increases in the cerebral blood flow of infants during low-pressure laparoscopy despite hyperventilation and having the patients in a head up position *(54)*. Laparoscopy is thus contraindicated in patients with head injuries or intracranial space occupying lesions *(55)*.

Another caveat pertains to patients with myelodysplasia, who in addition to their neurological disabilities often need substantial urological management. As the envelope continues to be pushed in paediatric urology these patients stand to benefit from an increasing number of complex surgical procedures that can now be completed laparoscopically, especially with the advent of robotics. A majority of these patients have, however, an associated Arnold-Chiari malformation obstructing the outflow from the fourth ventricle and requiring ventriculoperitoneal (VP) shunting for management of their obstructed hydrocephalus. Concern levelled at creating PnP in these patients has been rife, the obvious worry being that PnP may cause shunts to fail and in the worst case scenario lead to retrograde flow and pneumocephalus. Recent experience however shows that when adequate precautions are taken, presence of VP shunt need not be a contraindication. Clamping of the VP shunt, either intraperitoneally or by exteriorising the shunt, combined with regular exsufflation and pumping of the reservoir has been employed as a protective means *(56,57)*. Others reported the use of low pressures or invasive monitoring by measuring pressure directly from the shunt reservoir *(58,59)*. In the latter case the ICP increased rapidly to 25 mmHg upon insufflation and tapping of an average of 30 ml of cerebrospinal fluid was needed to restore ICP to what was deemed a safe level. Postoperative skull X-rays showed no evidence of pneumocephalus *(59)*. In the largest reported series of 18 patients with a mean age of 13 years, Jackman et al. using only non-invasive routine monitoring found no evidence suggesting clinically significant increases in ICP, and all procedures were completed successfully without event under an IAP of 12–20 mmHg *(60)*. VP shunts are designed with a one-way valve that only allows antegrade flow, this valve mechanism has been shown to withstand pressures of up to 350 mmHg before failing yet structural distortion occurs already at about 80 mmHg. Both pressures are well above the clinically used ranges of IAP *(61)*.

## 7. THERMOREGULATION AND METABOLISM

Paediatric patients undergoing operative procedures are prone to developing hypothermia. Hypothermia occurs due to the effects of general anaesthesia and the radiative, convective, and evaporative heat losses incurred to the ambient environment of the operating theatre. Furthermore, loss of temperature occurs due to the cooling effects of irrigation and intravenous fluids. Thermoregulation in neonates is further compromised by the inability of newborns to respond to cold exposure by shivering and the fact that general anaesthesia inhibits non-shivering thermogenesis. Maintaining normothermia intraoperatively is of utmost importance as hypothermia is known to significantly increase perioperative morbidity, a fact long recognized by paediatric surgeons, and which has lead to the institution of routine precautionary measures such as use of forced air warmers, warmed intravenous fluids, and regulated temperate ambient conditions *(62)*. In contrast to open procedures, laparoscopy can be envisaged to minimize heat loss as procedures are performed in the confines of a sealed abdomen which prohibits evaporative heat loss and retains the energy resulting from use of diathermy and other exothermic devices. This presumption is however contested by reports from adult, paediatric and animal studies which have repeatedly documented that hypothermia is not an infrequent occurrence in subjects undergoing laparoscopy *(1,18,20,63,64)*. Kalfa et al. reported core body temperatures <35 °C in 25% of their infant patients at the end of laparoscopic surgery despite using external heating sources. By using a linear regression model they found a significant inverse correlation between the length of surgery and core body temperature. Temperature loss was calculated to be 0.01 °C for each elapsed minute of surgery *(18)*. By comparing the heat loss sustained by infants undergoing open versus laparoscopic pyloromyotomy, Holland et al. showed that the drop in core temperature was more pronounced in the laparoscopic group although this difference did not reach statistical significance *(65)*. Heat dissipation in laparoscopy is mainly linked to insufflation of large amounts of non-humidified cold $CO_2$ and to a lesser extent to the use of irrigation fluids *(63,64)*. $CO_2$ is usually insufflated at room temperature and will in large amounts cool the internal organs and hence core temperature. This is further compounded in cases of gas leak where the constant circulation and exchange of cold dry insufflated $CO_2$ results in evaporative heat loss. Heating and especially humidifying the insufflant has been shown to significantly counteract such heat dissipation *(63)*. It is therefore imperative that working ports are properly secured and airtight so as to minimize the amount of insufflant needed, which in itself can be a challenge especially in neonates and micropremmies in whom the abdominal wall can be paper thin *(66)*.

## 8. SURGICAL STRESS AND IMMUNE RESPONSE

Laparoscopic surgery in both adults and children has been associated with superior cosmesis, less postoperative pain, and quicker convalescence when compared to open surgical procedures of similar surgical stress *(67–69)*. Other than the apparent difference in size of the surgical incisions, laparoscopy has been shown to significantly reduce surgical stress when directly compared to formal laparotomy and this is believed to be the main reason underlying these benefits. Using markers of surgical stress such as cytokines and C-reactive protein (CRP), studies in paediatric patients undergoing laparoscopy have shown a muted surgical response when compared to patients having open procedures with significantly less elevations of the proinflammatory IL-6 and CRP in the immediate postoperative period *(20,69)*. It has also been suggested that the obligate period of immunosuppression following surgery in children and which is characterized by decreased expression of class II Major Histocompatibility Complex (MHC) HLA-DR is less pronounced after laparoscopy *(70,71)*. MHC/HLA-DR plays an important role in processing and presenting bacterial antigens to T-Helper cells, so a decreased expression of this protein is associated with detrimental effects on the ability to combat postoperative infection, and the levels of expression which are inversely proportional to the magnitude of surgical stress have been directly correlated to postoperative outcome *(70,72)*.

Interest has recently focused on an unanticipated and for that matter unintentional immune modulating effect of laparoscopy. It is well established that the organism mounts an acute phase response in the face of surgery, trauma, or sepsis *(73)*. This response although mainly beneficial can overshoot and become overwhelming resulting in a systemic inflammatory response which if left unchecked leads to multiorgan failure and ultimately death *(74)*. In vivo and in vitro animal studies have shown that $CO_2$ PnP can attenuate this response by modulating the immune response to surgical trauma. This is mediated by a $CO_2$-dependent increase in levels of the anti-inflammatory cytokine IL-10 which in turn downregulates TNFα production. In vitro incubation of peritoneal macrophages in $CO_2$ demonstrated this as it resulted in less TNFα and proinflammatory IL-1 cytokine production in response to bacterial lipopolysaccharide (LPS) stimulation, than when macrophages were incubated in helium or air *(75)*. Similarly, it has been shown by Hanly et al. that induction of peritoneal sepsis by caecal ligation and puncture in rats resulted in an attenuation of the hepatic acute phase gene expression and preservation of circulating leukocyte volume in animals that had undergone the procedure laparoscopically using $CO_2$ PnP rather than helium or by means of laparotomy *(76)*. In another study by the same group, pre-treatment of rats by inducing a short period of $CO_2$ PnP effectively increased surgical survival after a subsequent LPS contaminated laparotomy procedure *(77)*.

PnP-mediated immune modulation is the result of the local peritoneal acidifying properties of $CO_2$, as such a response has only clearly been shown in association with the use of $CO_2$ insufflation. Instilling acid into the peritoneal cavity resulted in a similar reduction of the inflammatory response to LPS challenge *(78,79)*. Other studies have been less categorical in their conclusions stating merely that $CO_2$ PnP better preserves the status quo with regard to the immune modulating mechanisms and parameters assessed, in that the end result of some of the modulated immune processes can be viewed as either being beneficial or detrimental to the host depending on the held interpretation of the overall complex immune cascade *(80)*. The same holds true for the study by McHoney et al. in which it was shown that children undergoing laparoscopic fundoplication may have had an immunologic benefit over those undergoing open surgery, albeit not unequivocally *(71)*. It remains, however, that the immune modulating effect of $CO_2$ PnP is an interesting phenomenon that needs further elucidation not least within the clinical realm and may have potential exciting prospects in the management of acutely ill paediatric patients who up until now are preferentially managed by conventional open surgery should need arise.

## 9. EFFECT ON TUMOUR SEEDING

The issue of whether laparoscopy has a beneficial or detrimental effect on tumour cell behaviour continues to be debated. Initial reports from the adult literature seemed to suggest a higher incidence of port site metastases as compared to open surgery, but with increasing experience a decline in that incidence was noted and the initial gloomy results were attributed to a learning curve phenomenon. Conflicting outcomes between clinical and animal experimental studies have also added to the confusion; recent human studies have generally found a favourable effect of $CO_2$ PnP on tumour cell behaviour whereas animal studies have noted the opposite when adult human tumour cell lines were studied *(81,82)*. Laparoscopic surgery is believed to affect tumour cell behaviour in several ways. Mechanically, PnP may lead to aerosolization of tumour cells which tend to seed port sites where gas has a propensity to leak *(83)*. Technically, excessive tumour manipulation and instrument contamination may lead to an increased risk of seeding *(81)*, and as mentioned previously there is the immune modulating effect of PnP. The reduction in postoperative immune suppression enjoyed by laparoscopy patients may translate into a better ability to combat residual tumour or spillage. On the other hand $CO_2$ PnP has also been shown to adversely affect peritoneal macrophage activity and thus may lead to enhanced tumour spread *(80)*. The metabolic effect of the gas used has also emerged as an independent factor with studies showing that helium PnP may be superior to $CO_2$ with regard to inhibition of tumour cell proliferation both in vivo and in vitro *(84–86)*.

In a study by Schmidt et al. paediatric tumour cell lines of neuroblastoma, lymphoma, and hepatocellular carcinoma investigated in vitro showed significantly decreased proliferation when exposed to $CO_2$ for a short period of 2 hours. A similar exposure to helium decreased the tumour cell proliferation of neuroblastoma, lymphoma, and rhabdomyosarcoma. Both gases significantly altered tumour cell activity, and therefore the effects could not solely be ascribed to the pH modulating effects of $CO_2$ *(87)*. In vitro rat studies failed to reproduce these results as $CO_2$ PnP had no advantage over open surgery for retroperitoneally inoculated neuroblastoma cells *(88)*. Notwithstanding this, the same group reviewed 129 laparoscopic tumour-related procedures in children and found no instances of port site metastasis, this has since been confirmed by others *(89–91)*. Clinical implications of these phenomena remain however elusive and further studies are needed before the full extent of tumour cell modulating effects of PnP and the mechanisms involved are elucidated.

## 10. CONCLUSIONS

Abdominal gas insufflation in children as in adults prompts a chain reaction of physiological events that if overlooked could be detrimental to patients and outcomes. Understanding and appreciating these changes and their consequences by both surgeons and anaesthetists are key to safe successful laparoscopic surgery in children. And while most physiological alterations encountered relate to the immediate well-being of the patient, new interesting aspects continue to emerge which undoubtedly will have important clinical relevance in the not too distant future and may ultimately alter the conventional wisdoms held in paediatric minimally invasive surgery and select areas of paediatric genitourinary laparoscopy.

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