

## Reply: Perioperative cooling to prevent adhesion formation may be counterproductive for the clinical outcome

Sir,

We thank Persson and van der Linden for drawing attention to the potential harmful effects of a decreased core body temperature (Sessler, 2001) upon immunology, vascular supply, wound healing and risk of wound infection following colorectal surgery (Kurz *et al.*, 1996). This, moreover, has stimulated research on the pathophysiology of core body temperature decrease during anaesthesia, and methods were developed to prevent this. Since mice are unfortunately too small for peritoneal cooling without affecting core body temperature, our experiments might have given the impression that we aimed to decrease core body temperature to prevent adhesion formation. We, therefore, thank you for the opportunity to discuss this in greater detail.

Our mouse model experiments have been consistent with the concept that adhesions between surgical lesions are enhanced by mesothelial trauma, i.e. mechanical trauma (Schonman R *et al.*, 2009), desiccation (Binda *et al.*, 2006), hypoxia (less than 5 mmHg O<sub>2</sub> partial pressure) (Molinas *et al.*, 2001) or hyperoxia (more than 70 mmHg partial pressure) (Elkelani *et al.*, 2004). Touching and desiccation clearly affect the superficial layers only, whereas the CO<sub>2</sub> pneumoperitoneum causes superficial hypoxia of <100 µm in depth, as evaluated by histochemistry (unpublished data). We would therefore have preferred to cool the peritoneal cavity without affecting the core body temperature in order to confirm the hypothesis that mesothelial cells are more resistant to hypoxia at lower temperature. Unfortunately, subsequent experiments in larger animals will be necessary to prove this.

Certainly, the potential harmful effects of decreasing core body temperature will have to be evaluated and monitored closely organizing trials to translate the observations on mice experiments into clinical medicine. A full discussion of cooling only the abdominal cavity in human was beyond the scope of our original article, and in addition this would have been speculative to a large extent. We therefore restricted the discussion to the fact that adhesion formation increased exponentially with core body temperature in mice (Binda *et al.*, 2004, Binda *et al.*, 2006).

Cooling the peritoneal cavity directly contradicts the clinically widely used heating of CO<sub>2</sub> gas during endoscopic surgery. To the best of our knowledge, however, this protocol was introduced clinically with little evidence of a beneficial effect of temperature alone. Indeed, almost invariably cold and dry gas was compared with warmed and moistened, and little attention was given to the associated desiccation

shown clearly in the mouse model to increase adhesion formation (Binda *et al.*, 2006). Moreover, circumstantial evidence suggests that cooling the peritoneal cavity without affecting core body temperature might not have an important deleterious effect in women. For over 20 years, we have been using high-flow insufflators for smoke evacuation during CO<sub>2</sub> laser surgery (Koninckx and Vandermeersch, 1991). During the first years, dry and freezing cold CO<sub>2</sub> was used; later, we used the Thermoflator together with a humidifier. Since the tubing is not isolated, this results in CO<sub>2</sub> at room temperature but with 100% relative humidity because of condensation. Upon entry into the abdominal cavity, the CO<sub>2</sub> gas is heated up and intraperitoneal temperature ranges between 28°C and 34°C depending on the flow rate and the localization in the abdomen, given the compartmentalization of the peritoneal cavity (unpublished observations). Heating of the CO<sub>2</sub> is unavoidably associated with some desiccation, contributing in itself to the cooling of the peritoneal cavity. Although proper trials have not been performed to evaluate the effect upon wound infection, our incidence of wound infections has been negligible, below 0.5%, and this notwithstanding the really low peritoneal cavity temperatures and an abdominal wall which clinically felt cold. This low incidence of wound infection might be explained by the fact that the core body temperature remained unaffected during these surgeries.

Given the increased risk of wound infections with lower core body temperatures, we should consider the risk of increasing intraperitoneal infections, especially following full thickness endometriosis resection of the bowel. In our historical data collected over the last 20 years, of over 100 full thickness endometriosis resections and a peritoneal cavity temperature below 34°C, peritoneal infections have been rare; however, this might also have been a consequence of the systematic use of antibiotics. In order to avoid desiccation, the humidified CO<sub>2</sub> gas should preferably be cooled slightly upon entrance, thus causing some condensation. For this reason, we consider the peritoneal cavity cooling should be performed by a third and independent means. Preliminary observational data indicate that in absence of desiccation, peritoneal temperatures at least as low as 29°C will not affect core body temperature suggesting that cooling is fairly superficial. Indirectly, this also seems to confirm that desiccation has a major contribution to cooling core body temperature.

The key question remains—what would be the optimal pneumoperitoneum temperature to decrease adhesion formation without serious adverse side effects. At present, we can only speculate. Adhesion formation decreased with temperature in mice (Binda *et al.*, 2004) with most of the effect observed at 32°C (Binda *et al.*, 2004, 2006). This, together with the observations of the intraperitoneal temperatures during our endoscopic surgery, might suggest an ideal intraperitoneal temperatures range between 28°C and 34°C. Only constant and controlled cooling will allow detailed investigation

of the relationship between peritoneal temperature and temperature gradients in intraperitoneal organs and the eventual risk of peritoneal infections. In conclusion, we postulate that we should distinguish clinically between the effects of even slight core body hypothermia (Kurz *et al.*, 1996; Sessler, 2001) and surgical conditions that do not affect the core body temperature, such as traditional laparoscopy with some desiccation and some decrease of pneumoperitoneum temperature. The effects of a pneumoperitoneum with a decreased peritoneal temperature without desiccation should be investigated in rigorous clinical trials.

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