

### The role of the peritoneal cavity in adhesion formation

The article by Barcz et al. (1) deserves a comment since it should make us think.

Differences in peritoneal fluid constituents between women with and without endometriosis have been studied repetitively since the late 1970s in order to gain insight into the pathophysiology of endometriosis and associated infertility. Endometriosis is associated with a low-grade inflammation with more and more activated macrophages in peritoneal fluid. Despite the huge amount of data available, as this article also contributes to the data of cytokine concentrations, a comprehensive conclusion was never reached. More specifically, for most factors it remains speculative which are contributing to the development of endometriosis and which are a consequence of endometriosis (2).

Peritoneal adhesions following surgery remain a major problem leading to chronic pelvic pain, infertility, and occasional bowel obstructions. The use of barriers to prevent adhesion formation was based on the prevailing concept that peritoneal healing and adhesion formation is decided in a few days, resulting from a local inflammatory process between opposing lesions. In this process, fibrin deposition and fibrinolysis play a major role. Efficacy of a barrier, however, rarely exceeded fifty percent. Recent evidence has demonstrated the importance of the entire peritoneal cavity and of factors in peritoneal fluid to enhance adhesion formation. While peritoneal lesions and the associated local inflammatory reaction remain essential to start the process, factors from the peritoneal cavity are quantitatively much more important for the severity and extend of adhesion formation. That slight manipulation of bowels in the upper abdomen can increase adhesions at a surgical lesion in the lower abdomen unequivocally points to factors from the upper abdomen reaching the lower abdomen through the peritoneal fluid (3). A series of experiments in a laparoscopic mouse model pointed to an acute inflammation of the entire peritoneal cavity as the driving mechanism (4). This acute inflammatory reaction is caused by the cumulative mesothelial trauma either mechanically or by mesothelial hypoxia (CO<sub>2</sub> pneumoperitoneum) (5) or hyperoxia (exposure to air, as in open surgery), or desiccation. Prevention thus should aim at a mesothelial partial oxygen pressure between 10 and 70 mmHg (achieved by adding a few percent of oxygen to the CO<sub>2</sub> pneumoperitoneum), while preventing any desiccation. Slight cooling of the peritoneal cavity is beneficial, since the mesothelial cell becomes more resistant to trauma. It should be realised that in order to combine absence of desiccation and cooling, the latter should be performed independently (e.g. by sprinkling saline at room temperature). If the temperature of the incoming humidified gas is slightly higher condensation will occur. If the temperature of the incoming gas is lower than the peritoneal temperature it will be heated and desiccation will occur.

Since both mechanisms of adhesion formation are complementary (local inflammatory process enhanced by factors from the peritoneal cavity), prevention should address both mechanisms. In animal models (6) and in the human (in preparation)

the sequential minimalization of mesenchymal damage during surgery (by cooling directly—absence of desiccation and an adequate gas mixture) while using a barrier after surgery leads to an efficacy of over ninety-five percent.

The article by Barcz et al. (1) is, to the best of our knowledge, the first to investigate the human factors in peritoneal fluid that might be involved in adhesion formation. Considering the model of the associated acute inflammation, it is not surprising adhesions are associated with increased IL-6 (and IL-1) concentrations. It is surprising adhesions are associated with a lower VEGF concentration because angiogenesis consistently has been considered adhesionogenic. Today we can only speculate about the exact mechanisms whereby peritoneal fluid factors enhance adhesion formation. Understanding these mechanisms, however, is bound to lead to new methods to prevent adhesion formation.

Barcz and colleagues (1) underline the importance of careful observation and precise reporting in clinical research. Undertaken to investigate the pathophysiology of endometriosis, their article ends up being very important to our understanding of adhesion formation.

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