

13. Renz CL, Laroche D, Thurn JD, Finn HA, Lynch JP, Thisted R, Moss J: Tryptase levels are not increased during vancomycin-induced anaphylactoid reactions. *ANESTHESIOLOGY* 1998; 89:620-5

14. Fisher MM, Baldo BA: Mast cell tryptase in anaesthetic anaphylactoid reactions. *Br J Anaesth* 1998; 80:26-9

15. Laroche D, Vergnaud MC, Sillard B, Soufarapis H, Bricard H: Biochemical markers of anaphylactoid reactions to drugs: Comparison of plasma histamine and tryptase. *ANESTHESIOLOGY* 1991; 75:945-9

16. Lynch JP, Renz CL, Laroche D, Moss J: Value of baseline tryptase levels in assessing tryptase release. *Inflamm Res* 2000; 49(suppl): S23-4

17. Moss J: Are histamine-releasing drugs really contraindicated in patients with a known allergy to drugs? *ANESTHESIOLOGY* 1993; 79:623-4

18. Mertes PM, Laxenaire MC: Allergic reactions occurring during anaesthesia. *Eur J Anaesthesiol* 2002; 19:240-62

19. Fisher MM, Baldo BA: The incidence and clinical features of anaphylactic reactions during anaesthesia in Australia. *Ann Fr Anesth Reanim* 1993; 12:97-104

20. Moss J, Roizen MF, Nordby EJ, Thisted R, Apfelbaum JL, Schreider B, McDermott DJ: Decreased incidence and mortality of anaphylaxis to chymopain. *Anesth Analg* 1985; 64:1197-201

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Thoracic Epidural Anesthesia

More than Just Anesthesia/Analgesia

SPLANCHNIC hypoperfusion following low systemic perfusion due to trauma, hemorrhage, or circulatory shock is thought to form part of the host response to these types of injury. At the level of the microcirculation, hypoperfusion may result either from redirection of blood flow away from the splanchnic organs, mediated by increased sympathetic activity, or from impaired blood flow distribution within the microvascular networks. Because splanchnic hypoperfusion is considered to be important in the development of increased mucosal permeability, endotoxemia, and organ failure, the adequacy of gastrointestinal perfusion has become a major concern in high-risk surgical and critically ill patients.¹ The importance of this concept is further emphasized by the observation that gastrointestinal hypoperfusion is also associated with increased mortality rates in such patients.^{2,3}

In the current issue of *ANESTHESIOLOGY*, Adolphs *et al.* report the results of a carefully conducted experimental study on the effects of thoracic epidural block on gut microvascular blood flow in a hemorrhage model in rats.⁴ The authors clearly demonstrate that thoracic epidural anesthesia (TEA) protected the gut from decreased microvascular perfusion and from increased leukocyte-endothelium interaction associated with insults due to hemorrhage/retransfusion. With regard to the effect of TEA on microvascular perfusion, most of the benefit was observed in the muscularis layer. Because sympathetic nerve fibers were detected in all layers of the gut except the mucosa, the authors argue that the favorable effects

of TEA on the microvascular perfusion of the muscularis layer must be explained primarily by the effects of the sympathetic block.

One important issue in the effect of TEA on splanchnic perfusion is the location of the epidural block. A complete sympathetic block in the splanchnic region is achieved only if the spread of the local anesthetic includes the thoracic sympathetic nerve fibers, which extend from T5 to T10. On the other hand, the epidural blockade of lumbar segments results in increased sympathetic activity in the splanchnic nerves due to a baroreceptor drive.⁵

Others have performed studies in the area. Ai *et al.* measured intramucosal pH in the ileum of rabbits to determine the effects of TEA (catheter tip at T8-10) during progressive hypoxia to an inspired oxygen fraction of 0.1.⁶ In their study, TEA slowed the progression of intestinal ischemia during hypoxia and conferred protection against an increase in portal endotoxin concentrations. Meissner *et al.* studied the effects of high thoracic epidural block (T1-5) on splanchnic blood flows using the microsphere technique in dogs.⁷ The thoracic block did not alter blood flow to the splanchnic organs in the study, but the splanchnic sympathetic nerves were not included in the epidural block. In another study, by Sielenkämper *et al.*, intravital microscopy was used to measure gut mucosal blood flow in the ileum of rats during TEA (catheter tip at T7-9).⁸ It was found that TEA increased mucosal blood flow and reduced irregular flow patterns such as stop-and-go flow in the capillary networks of the gut mucosa.

There is some supporting clinical information. In two studies, the effects of TEA in patients undergoing major abdominal surgery were determined using gastric tonometry.^{9,10} Both studies found that TEA prevented a decrease in intramucosal pH during surgery; however, in one study the exact location of the epidural block was not given.⁹ Mallinder *et al.* studied the effect of TEA (block T5-T11) on gastrointestinal blood flow in patients undergoing colorectal surgery.¹¹ These authors

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observed no beneficial effect of TEA on mucosal P_{CO_2} , intramucosal pH, or the P_{CO_2} gap. However, at all times, and independently of the type of anesthesia, parameters for mucosal perfusion were all within normal levels in most of the patients, thus suggesting that no mucosal hypoperfusion was present.¹¹ Two other studies reported the effects of epidural anesthesia on intramucosal gastric pH during aortic reconstruction surgery.^{12,13} No beneficial effects of epidural anesthesia on intramucosal gastric pH were observed, but measurements were performed in the stomach, whereas the epidural catheters were placed at L3–4 and T9–10, respectively. Therefore, it seems that in these two studies the epidural block did not necessarily include the upper splanchnic organs in which the effect of the intervention was measured.^{12,13}

In all of the experimental and clinical studies mentioned above, investigators who reported evidence of improved gastrointestinal perfusion associated with epidural anesthesia usually performed measurements within the region of the epidural block.^{6,8,10} whereas those who did not observe beneficial effects most likely conducted the measurements outside this area.^{7,12,13} It therefore seems that the current literature on this topic, although limited in extent, supports the view that a beneficial effect of epidural anesthesia on splanchnic blood flow can be expected only when care is taken to block the sympathetic nerve fibers that supply the splanchnic region.

Inasmuch as TEA does not increase cardiac output, the question is whether the effects of sympathetic block on splanchnic blood flow are due to a redistribution of blood flow within the splanchnic organs, or to an effect of TEA to increase the proportion of flow directed to these organs. Adolphs *et al.* observed a preferential improvement of blood flow toward the muscularis layer in their preparation. Because the gut mucosa lacked sympathetic innervation, the authors postulate that the sympathetic block was followed by a redistribution of flow within the gut wall.⁴ However, no direct evidence for this assumption is provided. In contrast to the work of the current authors, other investigators have reported an improvement in mucosal perfusion, both in experimental^{6,8} and clinical^{9,10} studies on TEA, thus arguing against a redistribution of blood flow away from the mucosa.

In an experimental study in rabbits, the epidural blockade of splanchnic sympathetic nerve fibers increased the diameter of venous capacitance vessels in the splanchnic region, whereas a lumbar epidural block was associated with reflex vasoconstriction of splanchnic vessels.¹⁴ Although changes in organ blood flow were not measured in absolute values, these observations suggest that a segmental epidural block will probably result in blood flow redistribution in favor of those organs within the sympathetic block and away from regions in which reflex vasoconstriction occurs.

The possibility cannot be excluded that TEA induces

quite complex hemodynamic changes—for example, by affecting the blood flow distribution both within and between organs. TEA also decreases endocrine metabolic responses and reduces the extent of sympathetic activity *via* a reduction in plasma catecholamine levels.^{15,16} It is possible that in addition to the segmental block of sympathetic nerve fibers, the decrease in plasma catecholamine levels attenuates a stress-related distribution of flow away from the splanchnic region. In addition, as discussed by Adolphs *et al.*, the possible effects of absorbed local anesthetic must be considered.⁴ The bottom line is that, currently, in view of the few published studies on this topic, the precise mechanisms underlying the effects of TEA on splanchnic blood flow remain unclear.

Another interesting finding of the study by the present authors is the observation that TEA prevented leukocyte-endothelium interactions caused by ischemia-reperfusion injury following hemorrhage and retransfusion. Although the possibility cannot be excluded that augmented hydrostatic forces, attributable to a higher microvascular flow rate, or antiinflammatory effects of absorbed local anesthetic, are partly responsible for the reduction in leukocyte adhesion, this finding could imply that TEA inhibited the inflammatory response to hemorrhage and retransfusion because of improved blood flow and a reduced extent of ischemia.

Other authors have reported that TEA protected against bacterial translocation when progressive hypoxia was used to establish splanchnic ischemia in rabbits.⁶ In critically ill patients with peritonitis, epidural analgesia using bupivacaine improved gastric mucosal perfusion and gut function in comparison with a control group of patients in whom morphine was given to provide analgesia.¹⁷ In view of these findings, it is tempting to postulate that TEA may not only be useful to prevent gut ischemia, but it could also be beneficial to protect against ischemia- or infection-related inflammatory responses originating from the splanchnic region. It is an open question whether TEA might be capable of being used as an added therapeutic approach to prevent the exacerbation of systemic inflammatory processes—for example, in sepsis or acute pancreatitis. In both sepsis and acute pancreatitis, gut mucosal hypoperfusion is a typical finding and is regarded as being important in the development of multiorgan failure.^{18,19} Mesenteric vasodilation using TEA could be useful for preventing tissue injury, especially in conditions in which catecholamine therapy aggravates vasoconstriction in the splanchnic region.²⁰

When discussing the effects of TEA on sympathetic activity, it must be emphasized that the effects of the sympathetic block are, of course, not restricted to the splanchnic region. Another important effect of TEA is the reduction of efferent sympathetic outflow to the heart—a factor claimed to be responsible for a reduction

in the incidence of myocardial infarction in patients anesthetized using TEA.²¹

In summary, the study by Adolphs *et al.* is one of the first to have shown evidence that segmental epidural blockade may be useful in providing protection against splanchnic hypoperfusion under the conditions of ischemia and reperfusion. The exact mechanisms underlying this protection, and the potential therapeutic uses of TEA beyond its use as an anesthetic or analgesic technique, are matters for further investigation.

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References

- Jakob SM: Splanchnic blood flow in low-flow states. *Anesth Analg* 2003; 96:1129–38
- Doglio GR, Pusajo JF, Egurrola MA, Bonfigli GC, Parra C, Vetere L, Hernandez MS, Fernandez S, Paliza F, Gutierrez G: Gastric mucosal pH as a prognostic index of mortality in critically ill patients. *Crit Care Med* 1991; 19:1037–40
- Poeze M, Takala J, Greve JW, Ramsay G: Pre-operative tonometry is predictive for mortality and morbidity in high-risk surgical patients. *Intensive Care Med* 2000; 26:1272–81
- Adolphs J, Schmidt DK, Mousa SA, Kamin B, Korsukewitz I, Habazettl H, Schäfer M, Welte M: Thoracic epidural anesthesia attenuates hemorrhage-induced impairment of intestinal perfusion in rats. *ANESTHESIOLOGY* 2003; 99:685–92
- Meissner A, Rolf N, Van Aken H: Thoracic epidural anesthesia and the patient with heart disease: Benefits, risks, and controversies. *Anesth Analg* 1997; 85:517–28
- Ai K, Kotake Y, Satoh T, Serita R, Takedo J, Morisaki H: Epidural anesthesia retards intestinal acidosis and reduces port vein endotoxin concentrations during progressive hypoxia in rabbits. *ANESTHESIOLOGY* 2001; 94:263–9
- Meissner A, Weber TP, Van Aken H, Rolf N: Limited upper thoracic epidural block and splanchnic perfusion in dogs. *Anesth Analg* 1999; 89:1378–81
- Sielenkämper AW, Eicker K, Van Aken H: Thoracic epidural anesthesia increases mucosal perfusion in ileum of rats. *ANESTHESIOLOGY* 2000; 93:844–51
- Sutcliffe NP, Mostafa SM, Gannon J, Harper SJ: The effect of epidural blockade on gastric intramucosal pH in the peri-operative period. *Anaesthesia* 1996; 51:37–40
- Kapral S, Gollmann G, Bachmann D, Prohaska B, Likar R, Jandrasits O, Weinstabl C, Lehofer F: The effects of thoracic epidural anesthesia on intraoperative visceral perfusion and metabolism. *Anesth Analg* 1999; 88:402–6
- Mallinder PA, Hall JE, Bergin FG, Royle P, Leaper DJ: A comparison of opiate- and epidural-induced alterations in splanchnic blood flow using intraoperative gastric tonometry. *Anaesthesia* 2000; 55:659–65
- Väisänen O, Parviainen I, Ruokonen E, Hippeläinen M, Berg E, Takala J: Epidural analgesia with bupivacaine does not improve splanchnic tissue perfusion after aortic reconstruction surgery. *Br J Anesth* 1998; 81:893–8
- Piper SN, Boldt J, Schmidt CC, Maleck WH, Brosch C, Kumle B: Hemodynamics, intra-mucosal pH and regulators of circulation during perioperative epidural analgesia. *Can J Anesth* 2000; 47:631–7
- Hogan QH, Stekiel TA, Stadnicka A, Bosnjak ZJ, Kampine JP: Region of epidural blockade determines sympathetic and mesenteric capacitance effects in rabbits. *ANESTHESIOLOGY* 1995; 83:604–10
- Brodner G, Van Aken H, Hertle L, Fobker M, Von Eckardstein A, Goeters C, Buerkle H, Harks A, Kehlet H: Multimodal perioperative management—combining thoracic epidural analgesia, forced mobilization, and oral nutrition—reduces hormonal and metabolic stress and improves convalescence after major urologic surgery. *Anesth Analg* 2001; 92:1594–600
- Holte K, Kehlet H: Epidural anaesthesia and analgesia: Effects on surgical stress responses and implications for postoperative nutrition. *Clin Nutr* 2002; 21:199–206
- Spackman DR, McLeod AD, Prineas SN, Leach RM, Reynolds F: Effect of epidural blockade on indicators of splanchnic perfusion and gut function in critically ill patients with peritonitis: A randomised comparison of epidural bupivacaine with systemic morphine. *Intensive Care Med* 2000; 26:1638–45
- Sielenkämper AW, Meyer J, Kloppenburg H, Eicker K, Van Aken H: The effects of sepsis on gut mucosal blood flow in rats. *Eur J Anaesthesiol* 2001; 18:673–8
- Hynninen M, Valtonen M, Markkanen H, Vaara M, Kuusela P, Jousela I, Piilonen A, Takkunen O: Intramucosal pH and endotoxin and cytokine release in severe acute pancreatitis. *Shock* 2000; 13:79–82
- Hinder F, Stubbe HD, Van Aken H, Baba HA, Jahn UR, Brodner G, August C, Erren M, Booke M: Early multiple organ failure after recurrent endotoxemia in the presence of vasoconstrictor-masked hypovolemia. *Crit Care Med* 2003; 31:903–9
- Beattie WS, Badner NH, Choi P: Epidural analgesia reduces postoperative myocardial infarction: A meta-analysis. *Anesth Analg* 2001; 93:853–8