

### Intestinal Oxygen Consumption and Mucosal Damage during Ischemia-Reperfusion Injury

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**Introduction:** The intestinal mucosa is extremely susceptible to ischemia-reperfusion injury (IRI). Impairment of the mucosal barrier predisposes to bacterial translocation and septicemia. Therefore, we evaluated the influence of prolonged cold ischemia time (CIT) on the intestinal mucosa and oxygen consumption after reperfusion.

**Methods:** Porcine intestines were explanted after flushing with 4 L of HTK-solution. The intestines were stored at 4 °C in HTK for 2 (n=5; group A) and 20 h (n=5; group B). Thereafter, the intestines were reperfused with porcine blood in a closed circuit perfusion system. Arterial and venous blood were drawn every 30 min. Tissue samples were taken before and after HTK-perfusion, at the end of CIT and every hour after reperfusion. Oxygen consumption was measured as the product of arterio-venous difference and blood flow. The Chiu-classification was used for histological grading of the mucosal damage.

**Results:** The oxygen-consumption (mL/min/100g) in groups A (B) were 0.85±0.24 (0.59±0.12) at 60 min, 0.82±0.11 (0.62±0.16) at 120 min, 0.82±0.06 (0.64±0.15) at 180 min, 0.83±0.02 (0.05±0.09) at 300 min and 0.5±0.23 (0.12±0.07) at 420 min after reperfusion. Mucosal damage was graded 0.2±0.4 (0.4±0.5) at the end of CIT, 0.8±1.2 (2.2±0.7) at 60 min, 1.4±1.4 (2.8±1.2) at 120 min, 2.0±1.8 (2.6±1.0) at 180 min, 2.0±1.3 (3.4±0.8) at 300 min, and 3.2±1.17 (3.5±0.5) at 420 min after reperfusion.

**Discussion:** IRI leads to impaired microcirculation with decreased blood supply in the capillary network. Parks et al in 1986 discussed a redistribution of mucosal blood and oxygen supply towards the villus basis during IRI.

**Conclusion:** The decrease of oxygen consumption is associated with the grade of mucosal damage. The sequence of mucosal damage from the villus tips towards the crypts underlines the reported redistribution of blood and oxygen supply by Parks. Prolongation of CIT results in decreased oxygen consumption and predisposes to an increased mucosal damage after reperfusion.

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#### Effects of Antioxidant Drugs on Intestinal Wall Microflow in Ischaemia-Reperfusion Syndrome

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**Introduction:** Antioxidants have proved to be a useful tool for reducing both the mortality rate and the local damage to the gut in the intestinal reperfusion syndrome (RS). However, there is no evidence that the effect of these drugs is due to an improvement in the local perfusion of previously ischemic tissues. Moreover, it could rather be that those positive effects were the consequence of a systemic effect.

**Methods:** RS was induced by cross-clamping the superior mesenteric artery in Wag male rats (220 g). Microflow was assessed simulta-

neously in both proximal and distal jejunum and terminal ileum (laser-doppler microflowmeter, Oxford Optronix) during 60 s before, during and after clamping. The ischemic period was selected after checking 30, 60, 90 and 120 min. The effect of folic acid (2.5 mg/kg iv) was assessed in two groups of rats (60 and 120 min of ischemia).

**Results:** After a 30 min ischemic period, capillary flow is restored to nearly normal values. Following 60 and 90 min there is a constant recovery failure, restricted to the terminal ileum, whereas after 120 min, there is a complete disarrangement of microvascular flow. When administering folic acid in the 120 min group, although there was a neat improvement of both survival rate and mucosal damage, no positive effect could be observed on microvascular flow. However, the vehicle used (2 cc of saline) increased microflow during reperfusion. On the other hand, the antioxidant drug proved useful in recovering the capillary flow during reperfusion of terminal ileum after 60 min of ischemia.

**Discussion:** This experiment shows that there are important differences among the animal models used to study the RS in the gut (60 or 120 min). In fact, the folic acid, though being somehow effective in both models, is not able to exert a relevant effect on the capillary flow, when prolonging the ischemic insult.

**Conclusions:** The local effect of folic acid on capillary flow does not justify the reduction of the mucosal injury it induces.

### PP93

#### Vitamin E, Allopurinol and Preconditioning; Increase Apoptosis during Ischemia-Reperfusion in the Intestinal Wall

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**Introduction:** The intestinal wall is among the tissues being most sensitive to ischemia-reperfusion (IR) injury. Apoptosis has been identified after IR injury to the small bowel. The aim of our experiments was to study whether vitamin E, allopurinol (AP) and ischemic preconditioning (IP), well-known protective agents against the IR injury, increase or decrease the apoptotic activity in the intestinal wall during ischemia-reperfusion injury.

**Methods:** 20 mongrel dogs underwent median laparotomy, an approximately 30 cm long jejunum segment was selected and 30 min ischemia was produced by clamping the supplying vessels. In group "Vit E" (n=5): 25 mg/kg vitamin E was given im, which was followed by 30 min ischemia and 4 h reperfusion. Group "AP" (n=5): before the 30 min ischemia and 4 h reperfusion, 50 mg/kg allopurinol was infused into the external jugular vein. Group "IP". (n=5): the experiment started with 3 times 5 min ischemic period. It was followed by 30 min ischemia and 4 h reperfusion. Group "C" (n=5), control group: the ischemia was maintained for 30 min while the duration of reperfusion was 4 h. Following surgery intestinal biopsies were taken and stained with hematoxylin eosin (HE). The apoptotic activity of the intestinal wall samples was demonstrated by immunohistochemical methods using the Apoptag Kit (Oncor, Biomarker). Apoptotic index referring to all the positively stained nuclei per 50 well-oriented intestinal villi was also calculated. Differences between the groups were analysed with the student's t-test ( $p < 0.05$ ).

**Results:** HE staining demonstrated cellular debris on the surface of the intestinal mucosa in every group. Apoptosis was found to be most intensive at the tip of the villi. The apoptotic index was