



UniversityHospital Heidelberg
Department of General Surgery



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Mitten in der Medizin

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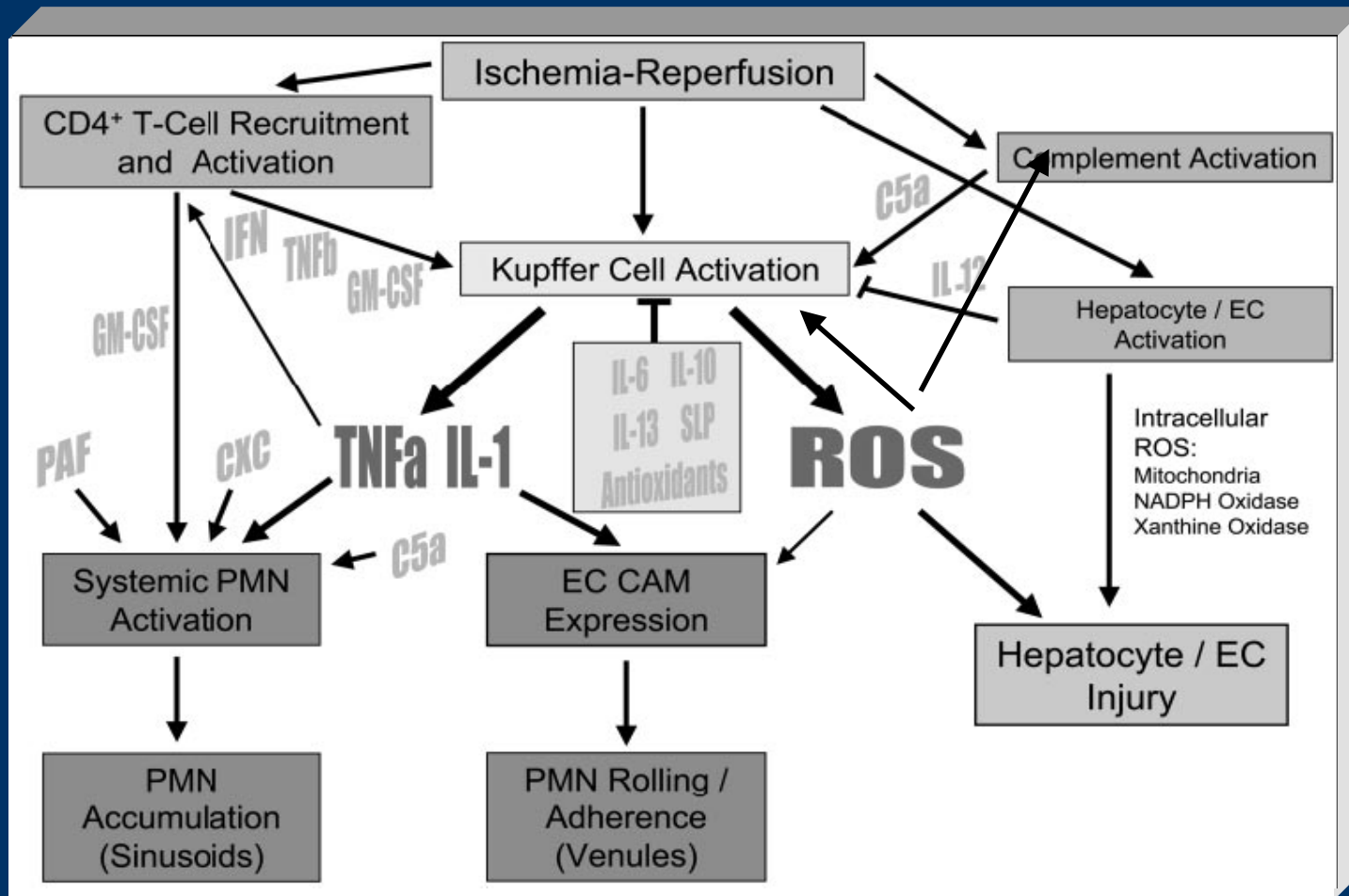
Gemeinsame Tagung von DGEM, AKE, GESKES und VDOE

Effects of a preconditioning oral nutritional supplement (pONS) on pig livers after warm ischemia

A. Nickkholgh, Z. Li, X. Yi, E. Mohr, S. Mikalauskas, L. Mikalauskiene,
M.L. Gross, M. Zorn, S. Benzing, H. Schneider, M.W. Büchler, P. Schemmer

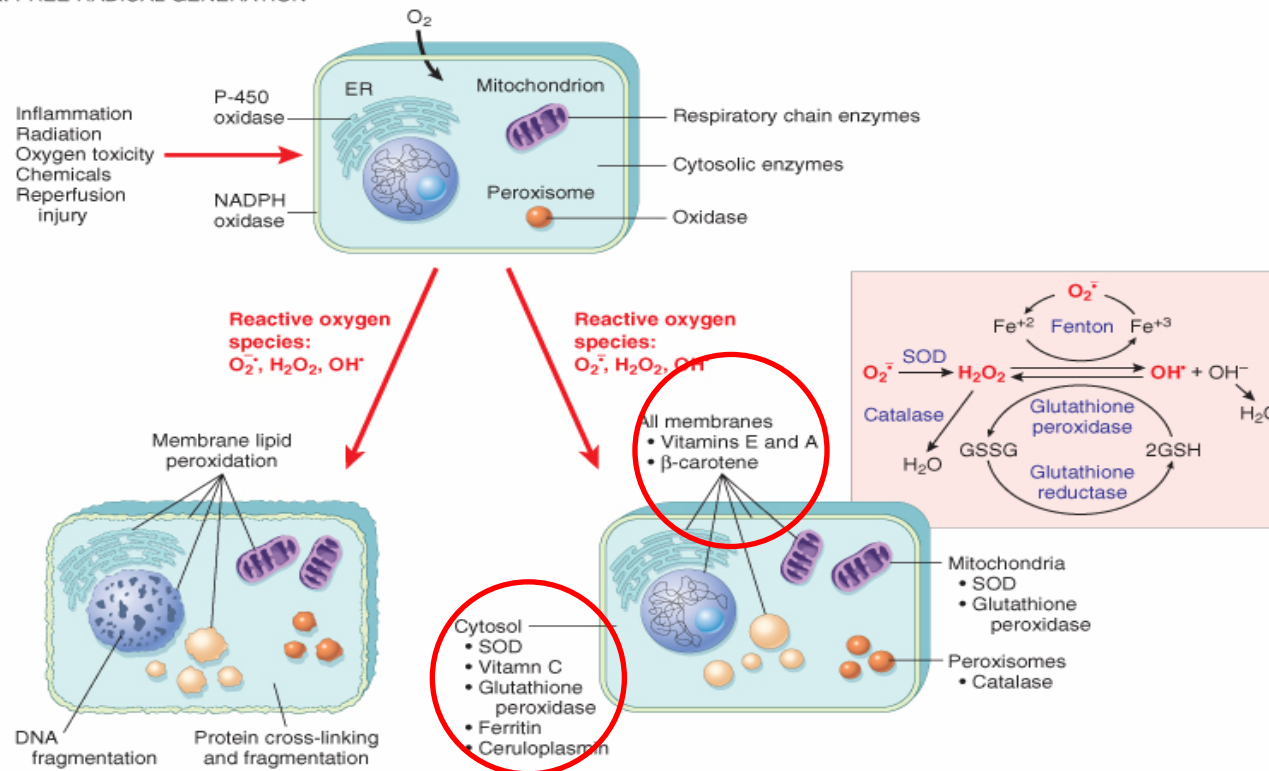


hepatic ischemia-reperfusion injury



Pharmacologic preconditioning

A. FREE RADICAL GENERATION



B. CELL INJURY BY FREE RADICALS

C. NEUTRALIZATION OF FREE RADICALS – NO CELL INJURY

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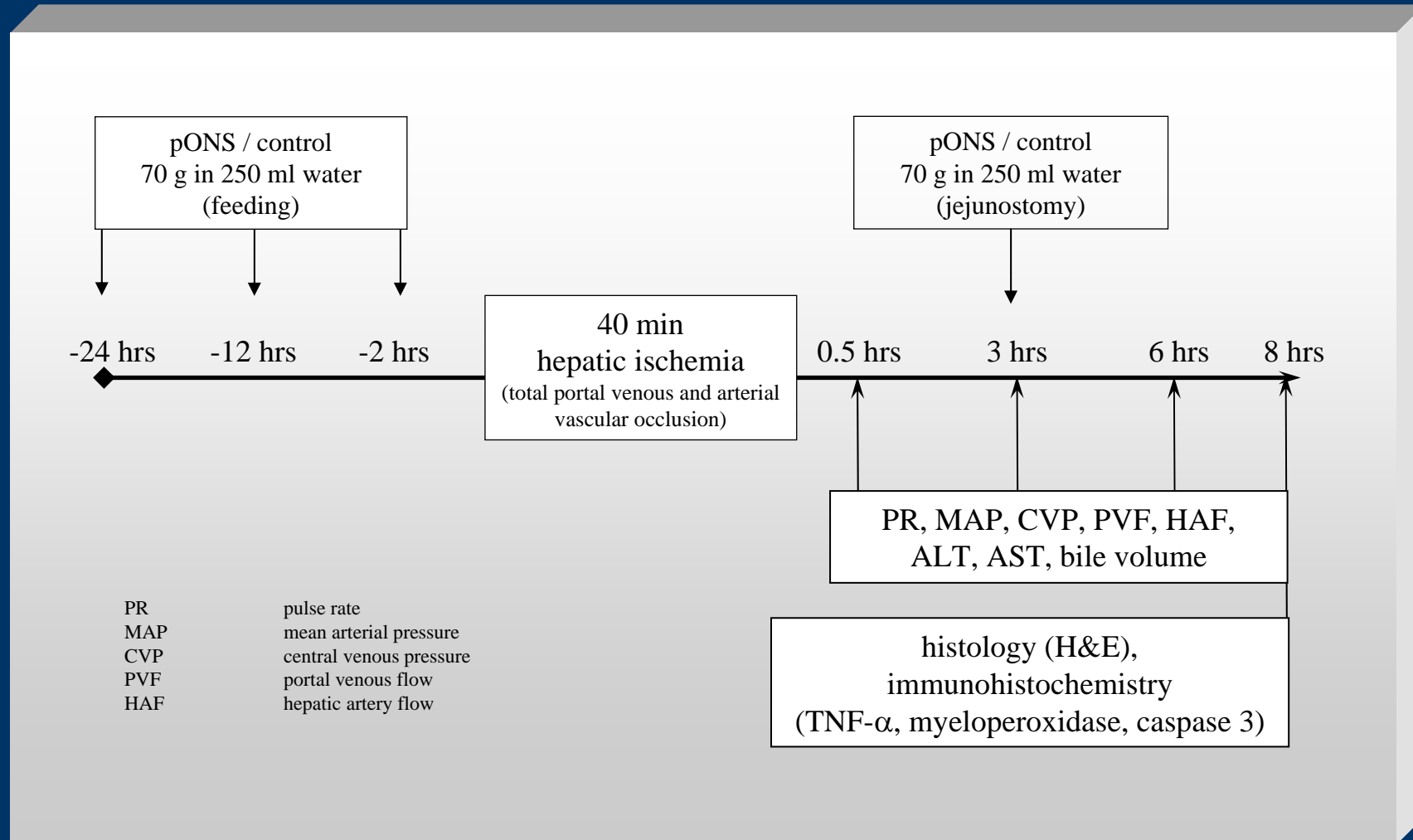
Warm ischemia of liver tissue

application of pONS (Fresenius Kabi)

- 70 g pONS in 250 ml tap water
 - glutamine (15 g), GTE (1 g; 99.3 % polyphenols), Vit. C (0.75 g), E (0.25 g), beta carotene (0.05 g), selenium (150 µg), zinc (0.1 g), carbohydrates (50 g)
- 24, 12, and 2 hrs before and 3 hrs after ischemia
- pre OP: feeding; post OP: jejunostomy



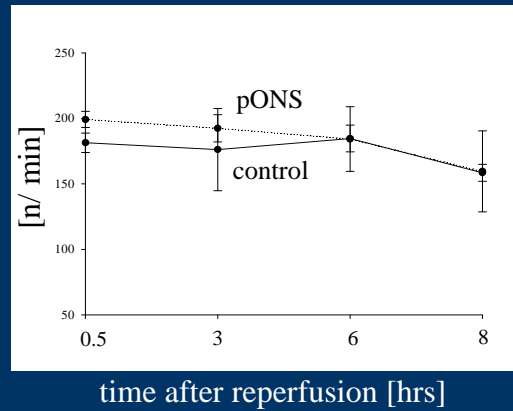
Protocol



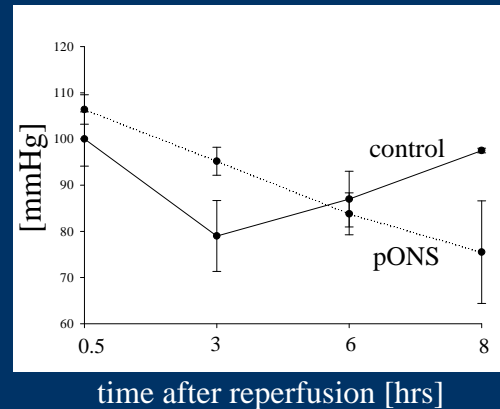


Hemodynamic parameters (1)

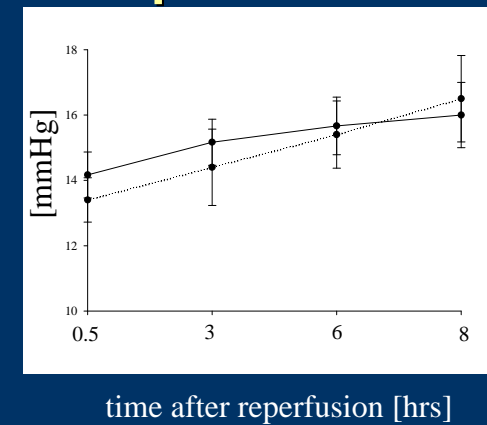
pulse rate



mean arterial pressure



central venous pressure



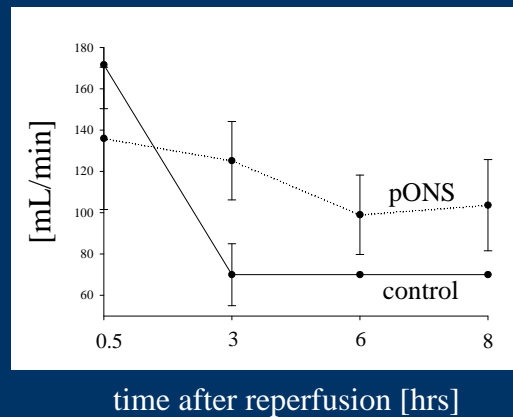
— control, n=6
..... pONS, n=5

values are Mean \pm SEM; * : $p < 0.05$

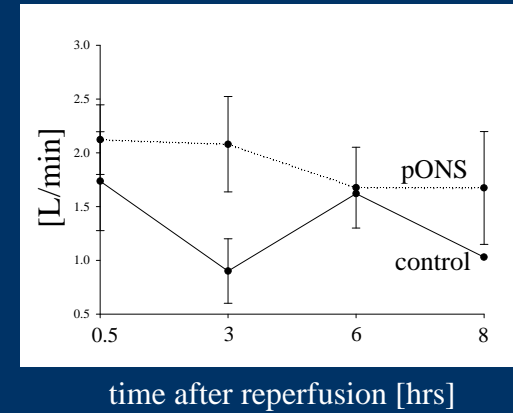


Hemodynamic parameters (2)

hepatic arterial flow



portal venous flow



— control, n=6

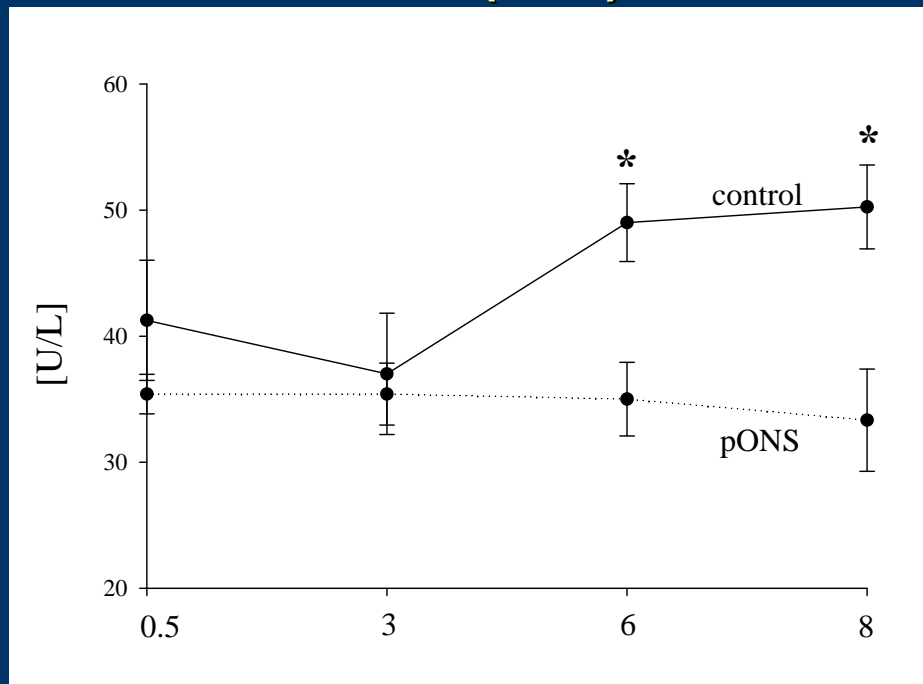
..... pONS, n=5

values are Mean \pm SEM; * : $p < 0.05$



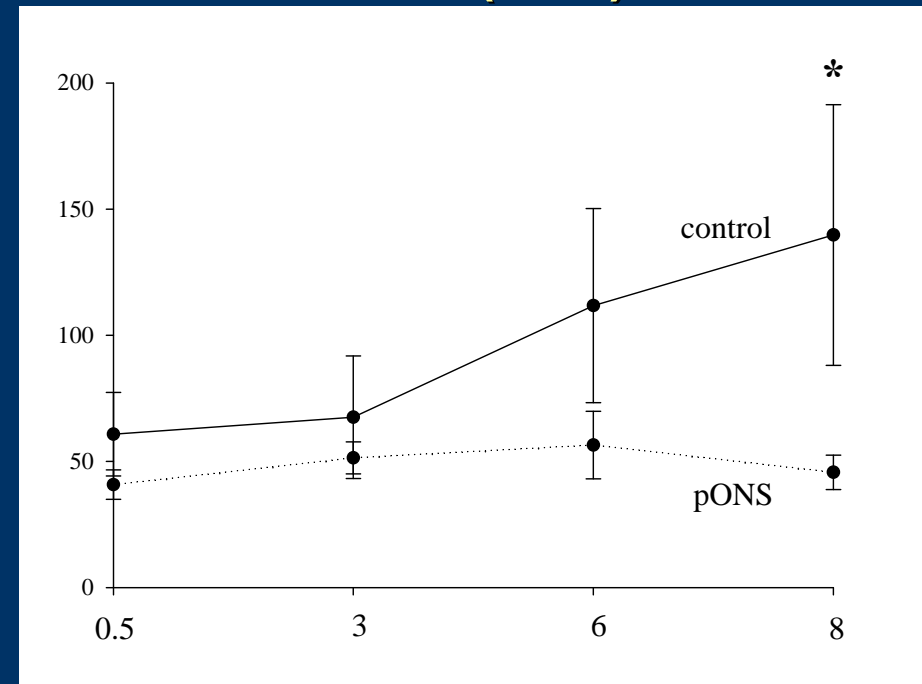
Transaminases

ALT (GPT)



time after reperfusion [hrs]

AST (GOT)



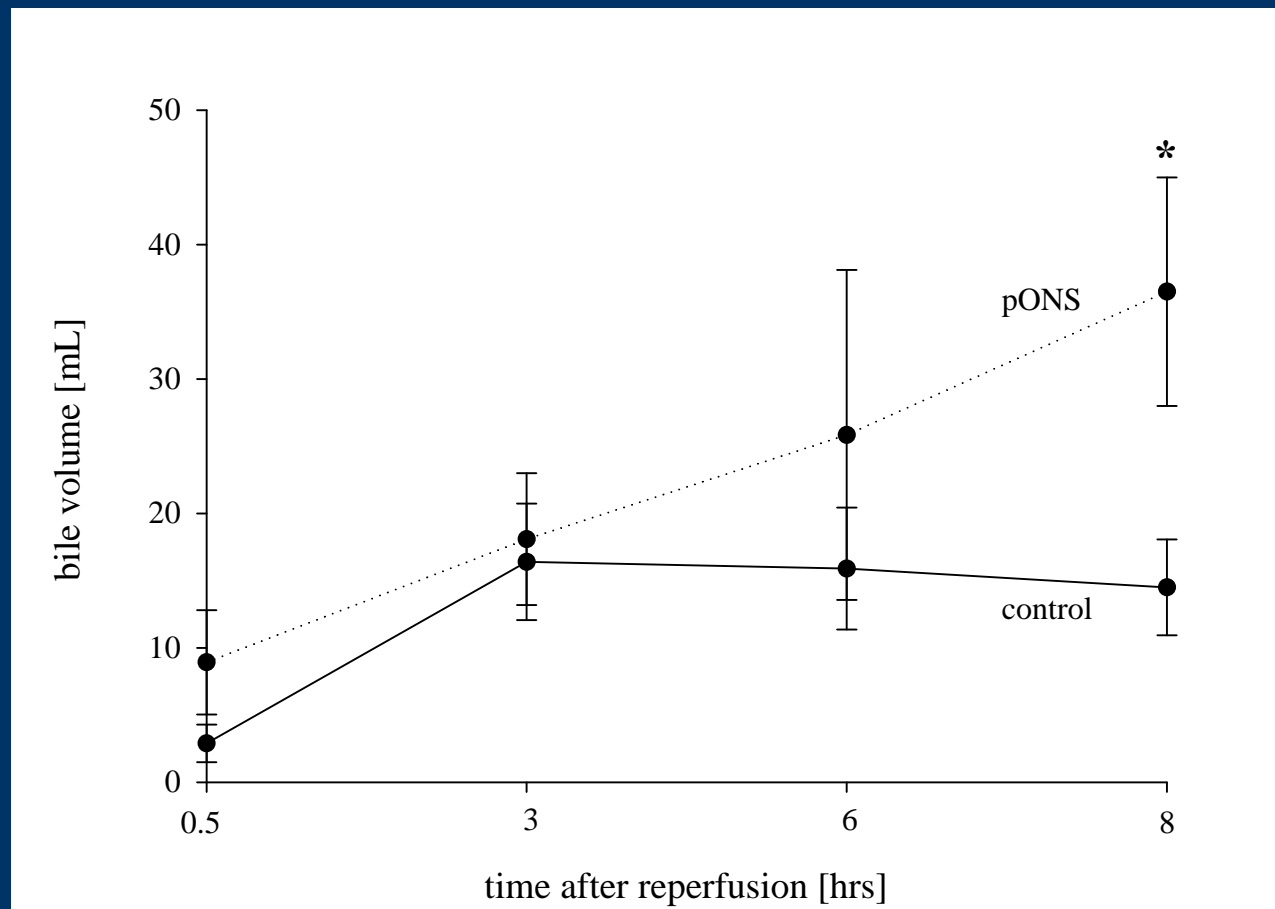
time after reperfusion [hrs]

— control, n=6
..... pONS, n=5

values are Mean \pm SEM; * : p < 0.05



Bile production



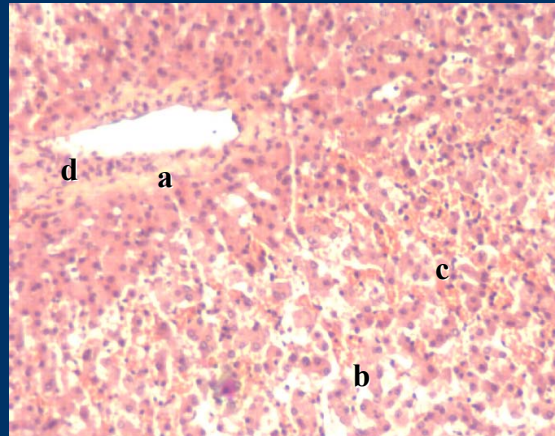
— control, n=6

..... pONS, n=5

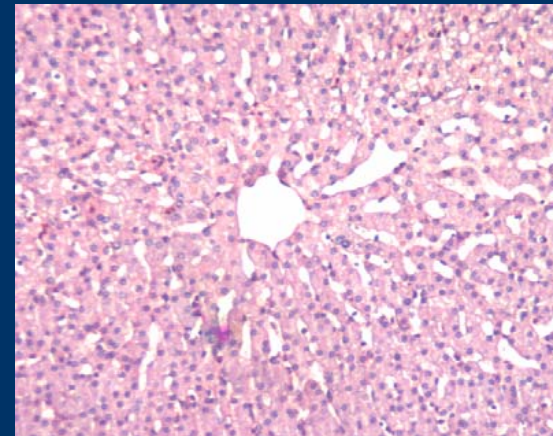
values are Mean ± SEM; * : p < 0.05



Histology, H&E staining (×100)



control



pONS

histopathology	Control				pONS				<i>p</i>
	n	Median	25%	75%	n	median	25%	75%	
necrosis	80	3	3	3	95	1	1	2	<0.001
leukocyte infiltration	80	4	3	4	96	1	1	2	<0.001

histomorphological changes:

grade 0, minimal or no evidence of injury;

grade 1, mild injury including cytoplasmic vacuolation and focal nuclear pyknosis;

grade 2, moderate to severe injury with extensive nuclear pyknosis, cytoplasmic hypereosinophilia, and loss of intercellular borders; and

grade 3, severe necrosis (a) with disintegration of hepatic cords (b), hemorrhage (c), and neutrophil infiltration (d).

To investigate leukocyte infiltration into the hepatic tissue, a scale from 1 to 4 was used:

grade 1, <10 leukocytes / field (focal infiltration);

grade 2, 10-20 leukocytes / field (mild infiltration);

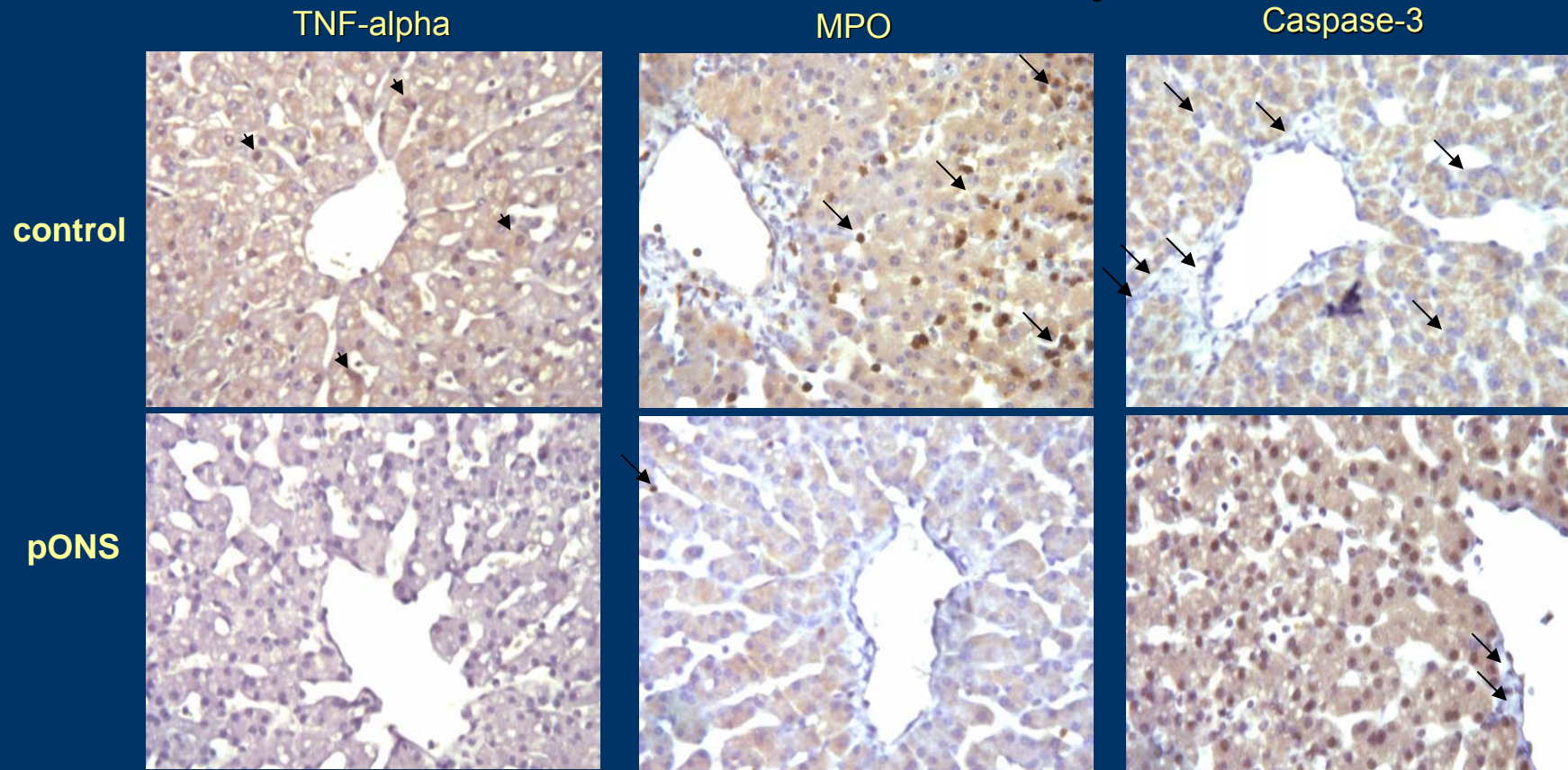
grade 3, 21-50 leukocytes/field;

grade 4, >50 leukocytes / field.

n; number of microscopic fields assessed



immunohistochemistry (×200)



expression	control				pONS				p
	n	median	25%	75%	n	median	25%	75%	
TNF- α	84	2	2	3	102	1	1	1	<0.001
MPO	79	4	3	4	99	2	2	3	<0.001
Caspase-3	81	4	3	4	100	2	1	2	<0.001

Immunohistochemistry was evaluated by the semiquantitative technique, relating the score of 0 to 4 points to the fraction of stained cells: 0, 0% cells; 1, <5% cells; 2, 5%-20% cells; 3, 20%-40% cells; 4, >40% positive cells.



Conclusion

- Oral pharmacologic preconditioning is feasible and beneficial.
- pONS protects liver from warm ischemia / reperfusion injury by decreasing:
 - *oxidative stress,*
 - *lipid peroxidation,*
 - *apoptosis, and necrosis.*



Dankeschön!

