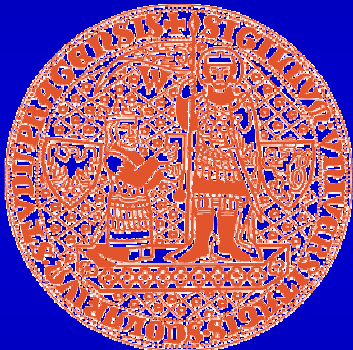


Metabolická odpověď kriticky nemocných - jak, kdy a proč zasahovat



Novák I.

JIP I. interní klinika FN Plzeň

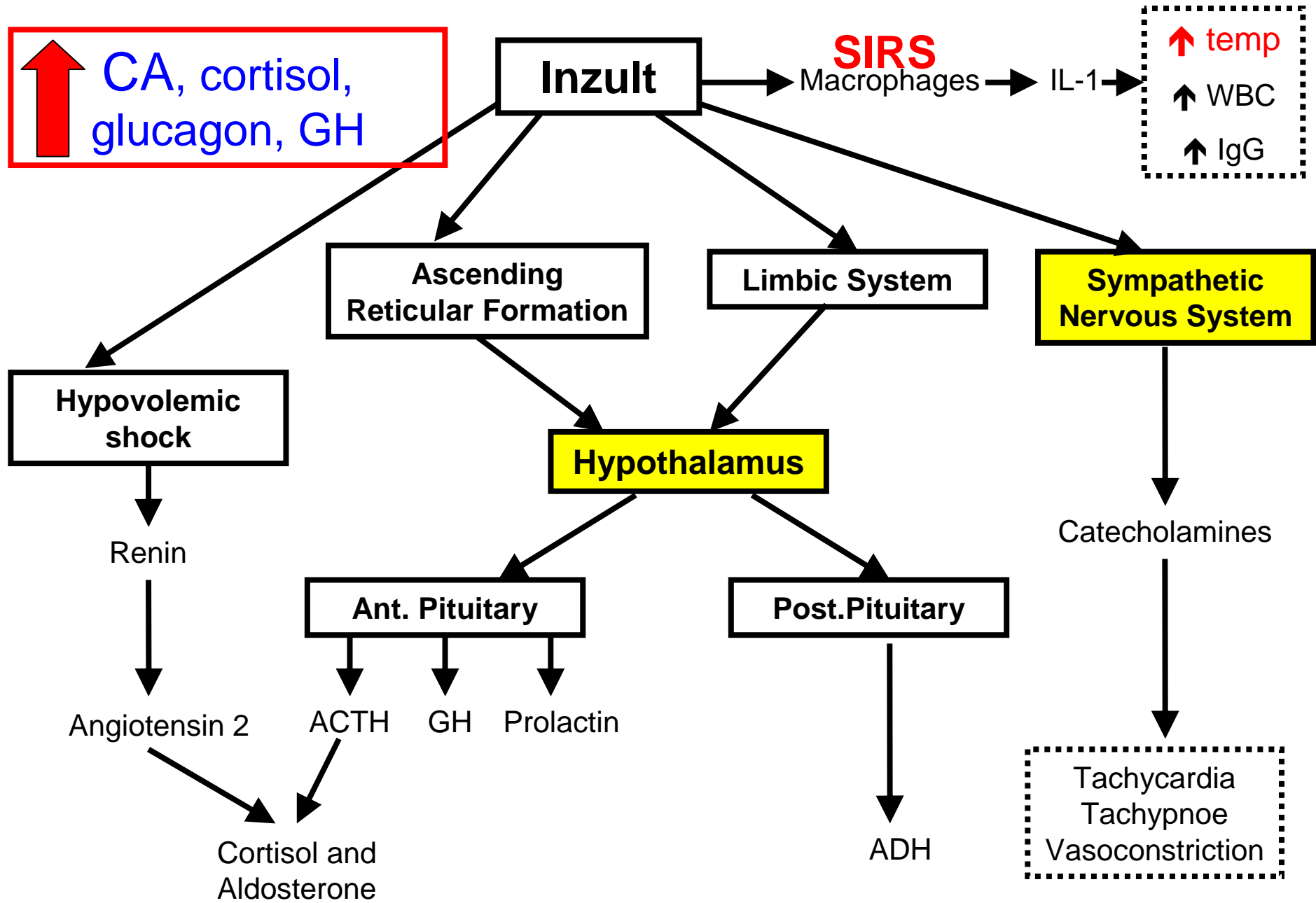
Inzult

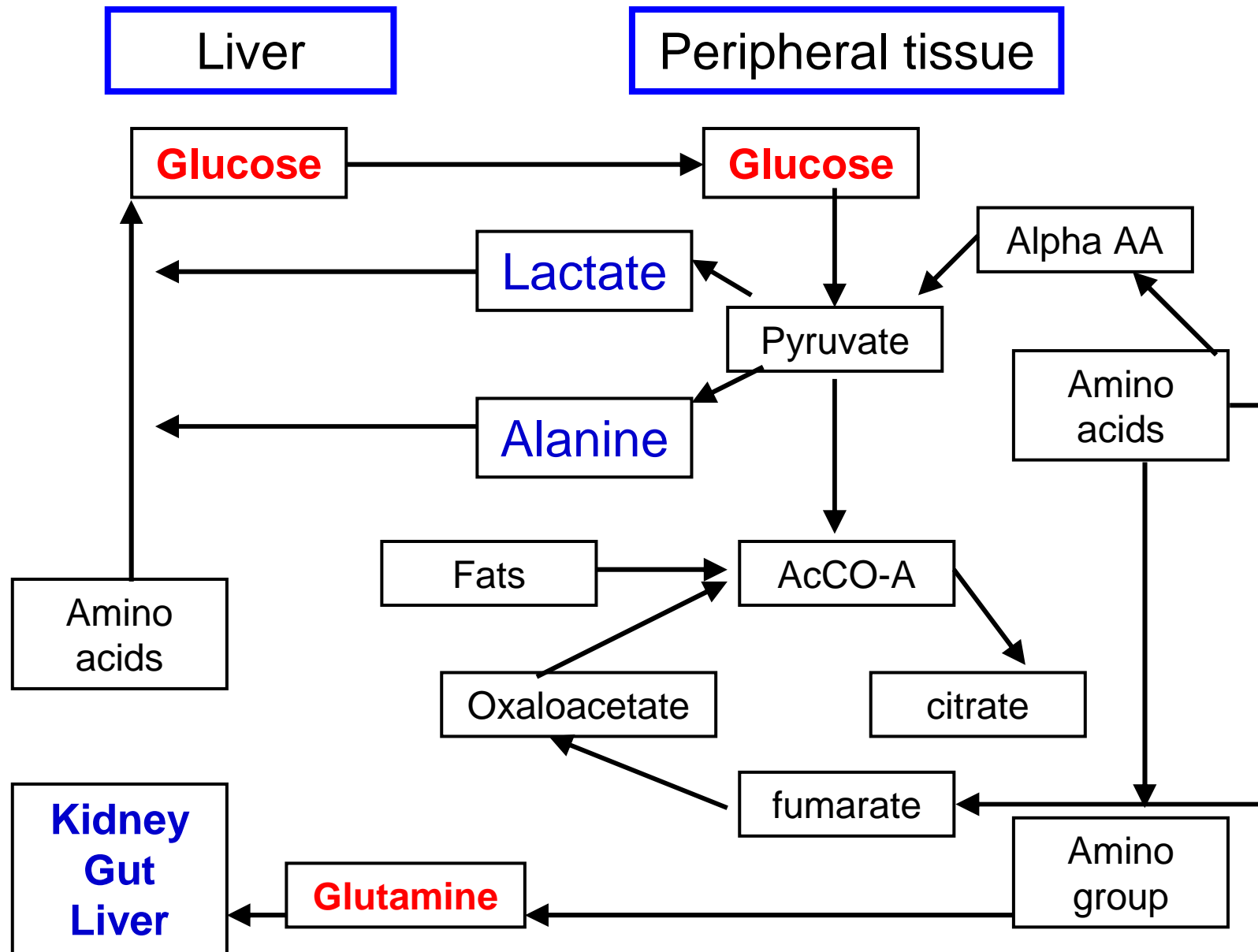
1. Intenzita inzultu
2. Délka trvání
3. Kardiovaskulární stav, nutriční stav, komorbidity
4. Terapeutické ovlivnění

Terapeutický management Priority

1. Hemodynamická stabilizace a kapilární recruitment
2. Kontrola infekce a ATB léčba
3. Kontrola homeostázy a hemostázy
4. Nutriční intervence
5. Minimalizovat iatrogenní poškození

Hormonal response to insult



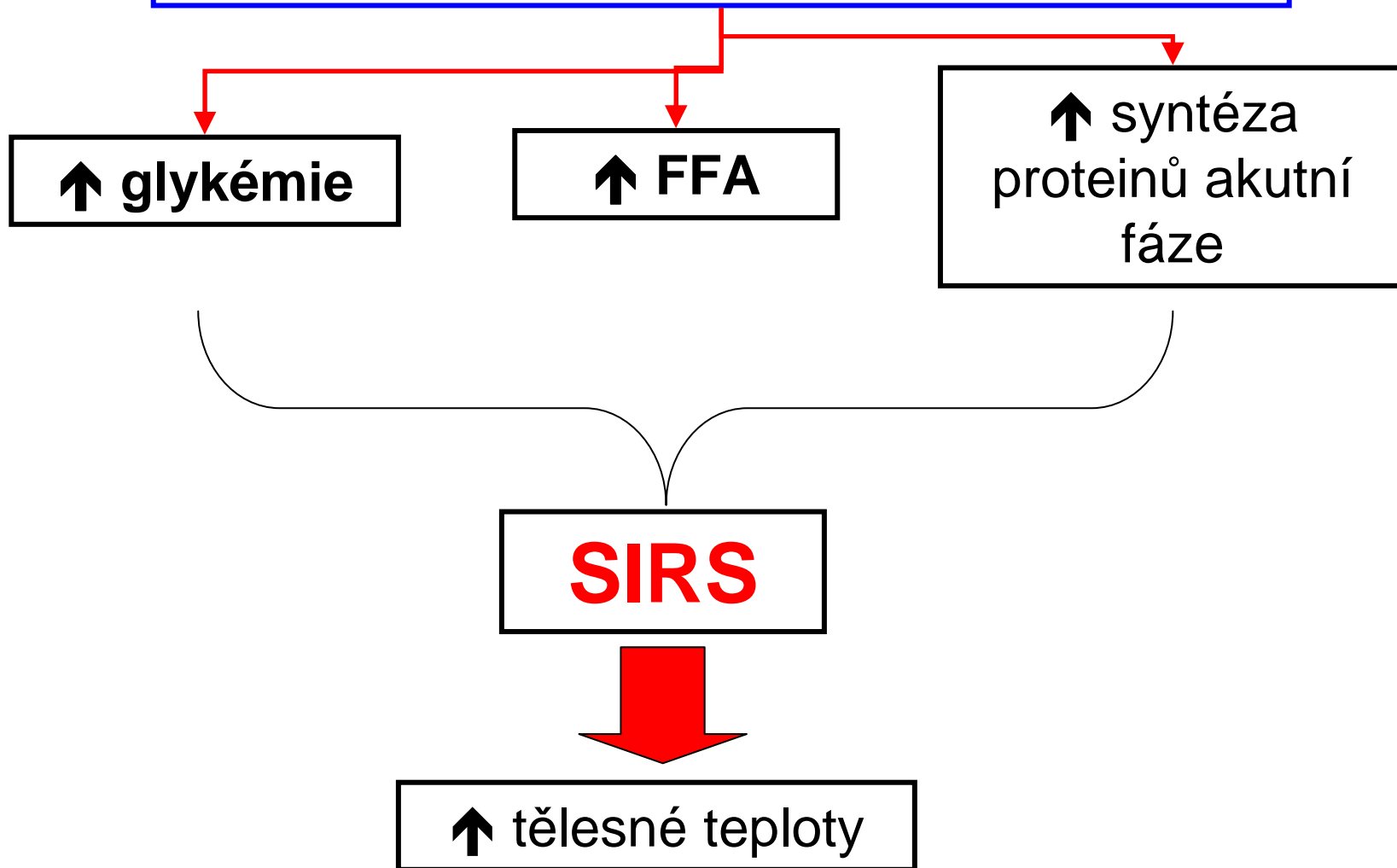


The endocrine response to critical illness is aimed to:

1. Maintain effective circulation
2. Maintain effective oxygenation
3. Increase generation of energy substrates: glucose, FFA and AAs from body stores: liver, muscles
4. Increasing synthesis of ATP (mitochondrial, non-mit)

VO₂ and EE are initially ↑ by up 200%

Inzult – metabolická odpověď

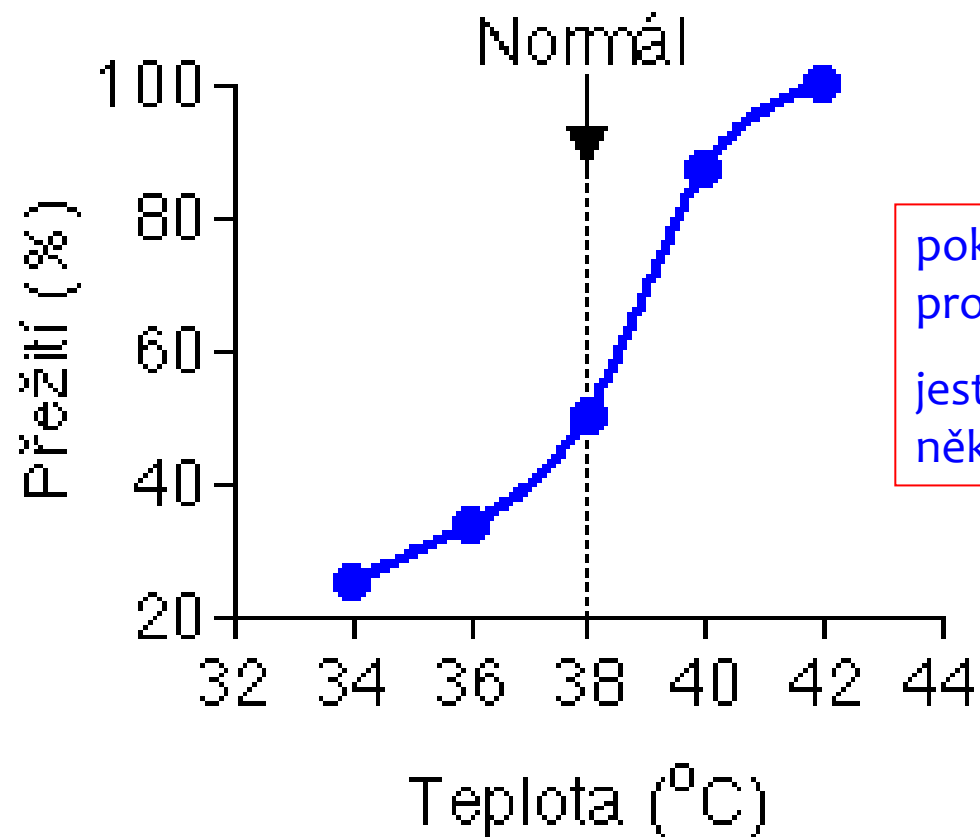


Přeladění termoregulace

Horečka

Fylogeneticky velmi stará (i bezobratlí), u poikilothermů změnou prostředí

Přestavení regulačního prahu k vyšším teplotám působením pyrogenů (IL-1)



pokus s infikovanými jestrkami držnými v prostředích o různých teplotách

jestěrky si horečku udělají tak, že vlezou někam, kde je tepleji

Čím to je?:

- zvýšená pohyblivost neutrofilů (fagocytují infekci)
- zvýšená produkce a protivirová a protibakteriální účinnost interferonu
- zvýšená proliferace T buněk

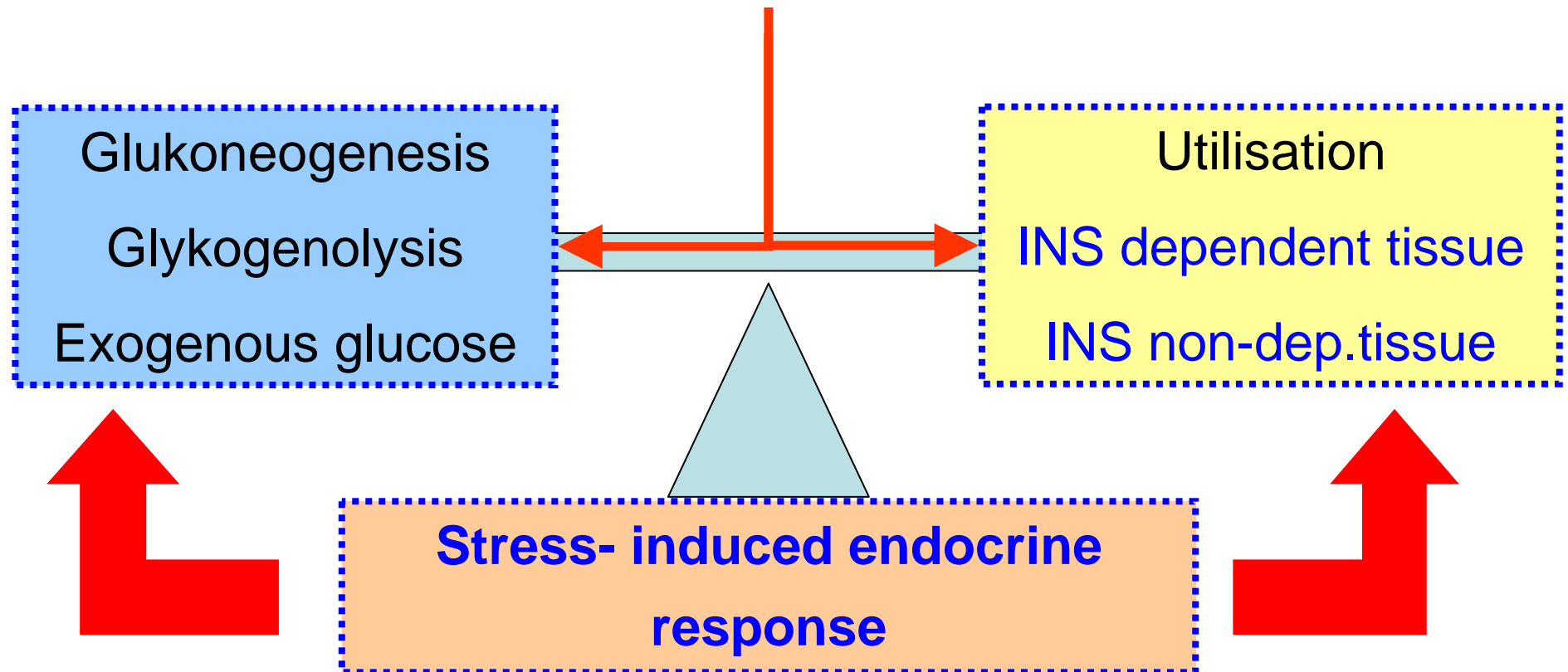
Hampl 2003

Metabolické změny

- **Metabolizmus glukózy**
- Metabolizmus MK
- Metabolizmus AMK

Glucose homeostasis and critical illness

Actual glycemias

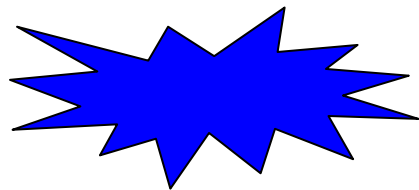


hypoglykémie

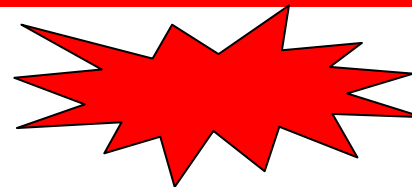
hyperglykémie

Proinflamatorní inzult

1. Délka trvání hypo- nebo hyperglykémie
2. Δ Glykémie od fyziol. rozmezí



Hyperglykémie „benignější“



Hypoglykémie rychlejší reakce
personálu

CAVE: nemocný sedovaný na ventilátoru !!!

The New England Journal of Medicine

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VOLUME 345

NOVEMBER 8, 2001

NUMBER 19



INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

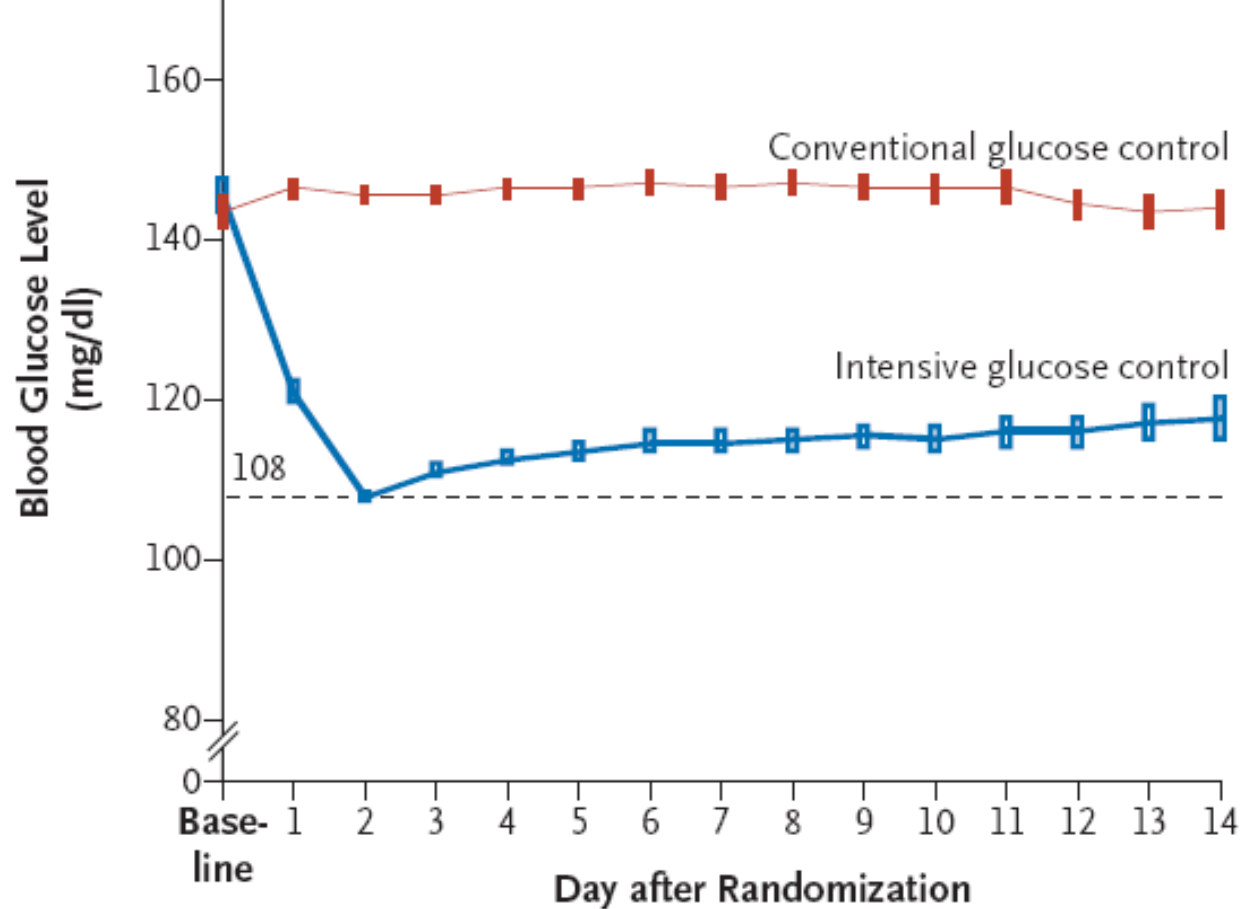
MARCH 26, 2009

VOL. 360 NO. 13

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*

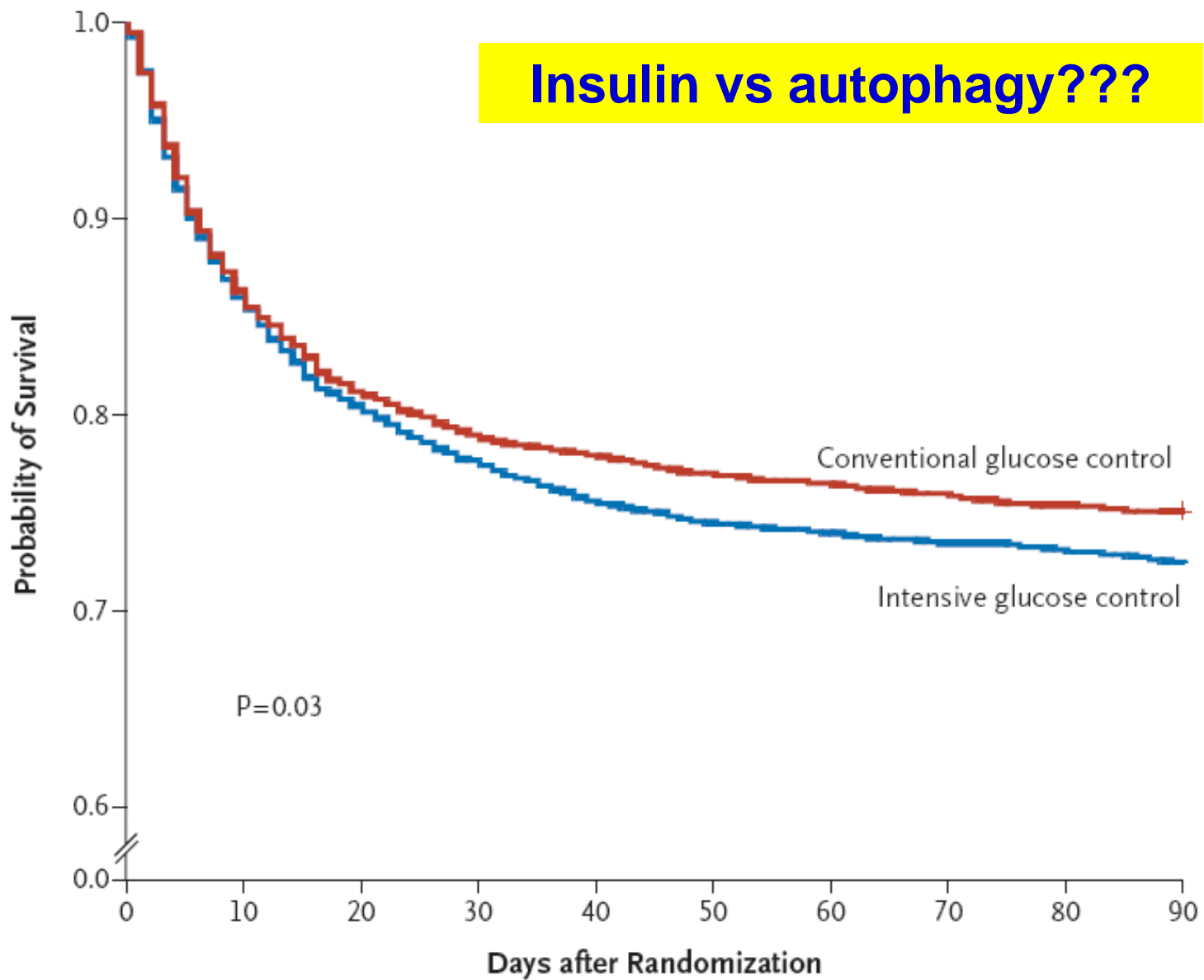
The mean time-weighted blood glucose values in the intensive-control group (6.4 ± 1.0 mmol/l) were significantly lower than those in the conventional-control group (8.0 ± 1.3 mmol/l; $P < 0.001$). Mortality in the intensive-control group was significantly higher than that in the conventional-control group (27.5% versus 24.9%, $P = 0.02$).



No. of Patients

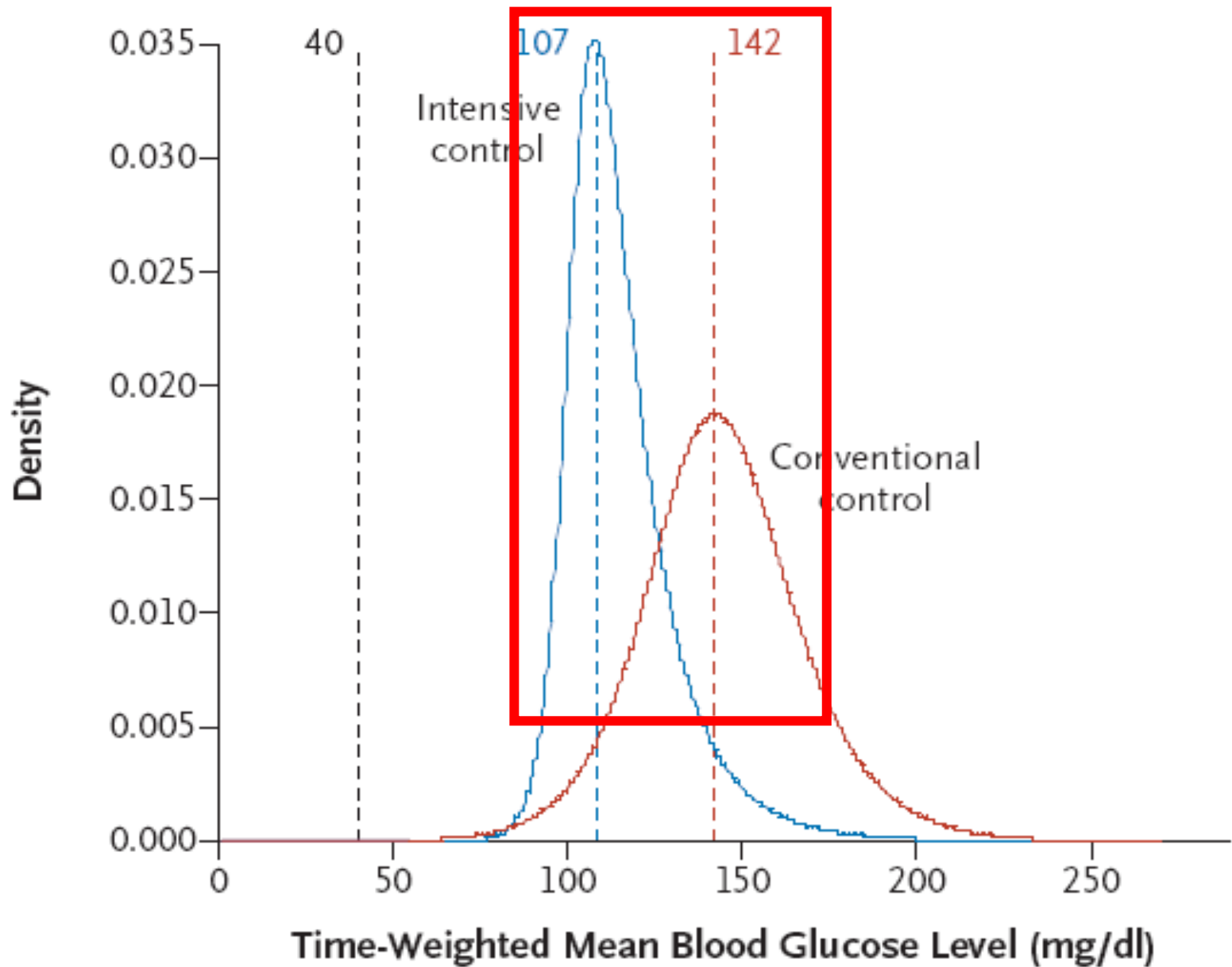
Conventional control	2995	2233	1380	909	583
Intensive control	2989	2260	1428	908	562

Insulin vs autophagy???



No. at Risk

Conventional control	3014	2379	2304	2261
Intensive control	3016	2337	2227	2182



Naše praxe = ITT 7 – 10 mmol/L

Autophagy in ischemic heart disease

- Autophagy – catabolic pathway by which mammalian cells degrade and recycle macromolecules and organelles
- Remove protein aggregates and damaged organelles
- Control of intracellular homeostasis

CAVE:

This pathway is upregulated under stress (ATP depletion, ↑ROS)

Autophagy is ↑ during ischemia and I/R trauma

Metabolické změny

- Metabolizmus glukózy
- **Metabolizmus AMK**
- Metabolizmus MK

Intestinal permeability and systemic infections in critically ill patients: Effect of glutamine*

Daurea A. De-Souza, MD, PhD; Lewis J. Greene, PhD

Crit Care Med 2005 Vol. 33, No. 5

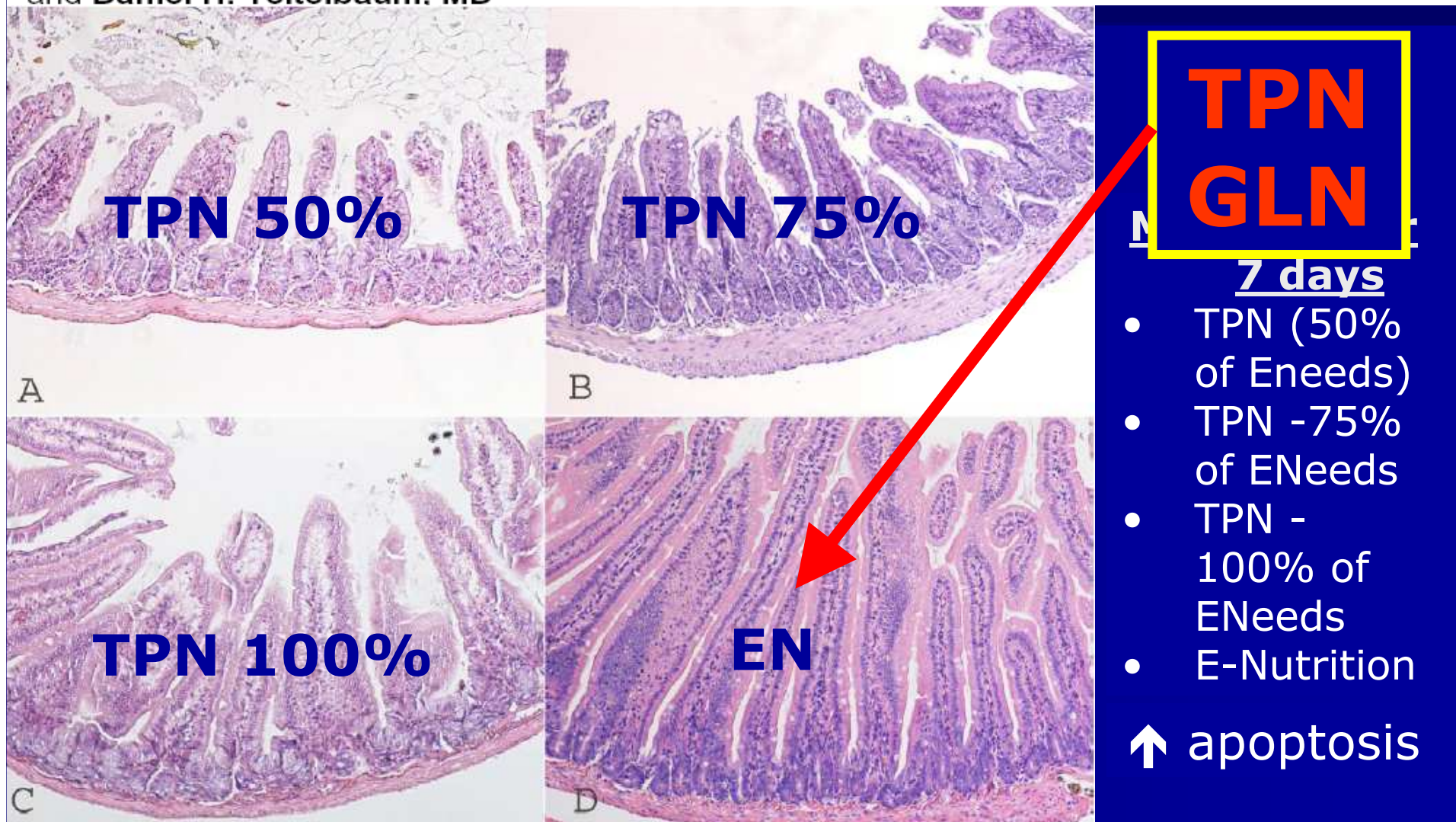
Effect of Glutamine vs. Type of Injury	Reference	Patients Under Study	Control Patients	Dose of Glutamine	Glutamine Administration Initiation Route Duration
"Protective" effect of glutamine in patients exposed to acute injury	Jiang et al (87)	60 patients undergoing major abdominal surgery	60 patients undergoing major abdominal surgery	0.50 g/kg/day of the alanine-glutamine dipeptide (Dipeptiven, Fresenius Kabi Bad Homburg, Germany), equivalent to 0.34 g glutamine/kg/day	1st day postsurgery Intravenous route 6 days
	Zhou et al (88)	20 patients exposed to severe burns	20 patients exposed to severe burns	0.50 g/kg/day of the alanyl-glutamine dipeptide (Ajinomoto, Tokyo, Japan) equivalent to 0.35 g L-glutamine/kg/day	1st day after burn Enteral route 11 days
		neoplastic disease	neoplastic disease		14 days
"Therapeutic" effect of glutamine in patients with chronic diseases	Noyer et al (90)	16 patients with AIDS (8 patients in each subgroup)	8 patients with AIDS	4 g or 8 g of glutamine/day	Outpatients in treatment for AIDS Oral route 28 days
	Den Hond et al (91)	7 patients with Crohn's disease	7 patients with Crohn's disease	21 g of glutamine/day (ICN Biomedicals, Cleveland, OH)	Patients in treatment for Crohn's disease Oral route 4 wks

Conclusions: Glutamine administration improves the prognosis of critically ill patients presumably by maintaining the physiologic intestinal barrier and by reducing the frequency of infections. (Crit Care Med 2005; 33:1125–1135)

IMPACT OF CALORIC INTAKE ON PARENTERAL NUTRITION-ASSOCIATED INTESTINAL MORPHOLOGY AND MUCOSAL BARRIER FUNCTION

JPEN J Parenter Enter Nutr. 2006 ; 30(6): 474-479.

Xiaoyi Sun, MD, PhD, Ariel U. Spencer, MD, Hua Yang, MD, PhD, Emir Q. Haxhija, MD, PhD, and Daniel H. Teitelbaum, MD



**TPN
GLN**

7 days

- TPN (50% of Eneeds)
- TPN -75% of ENeeds
- TPN - 100% of ENeeds
- E-Nutrition

↑ apoptosis

Efficacy of parenteral nutrition supplemented with glutamine dipeptide to **decrease hospital infections in critically ill surgical patients.**

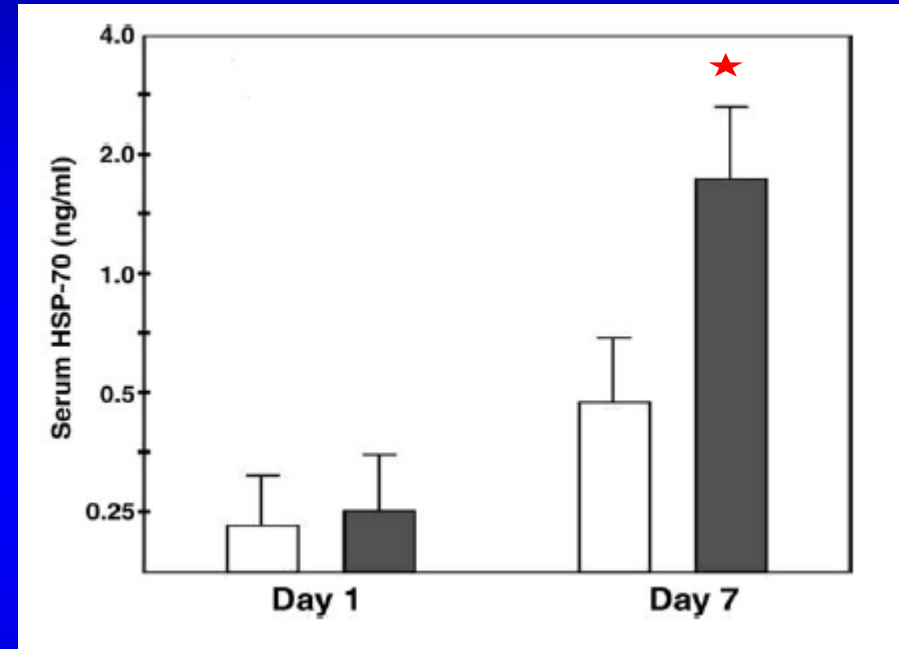
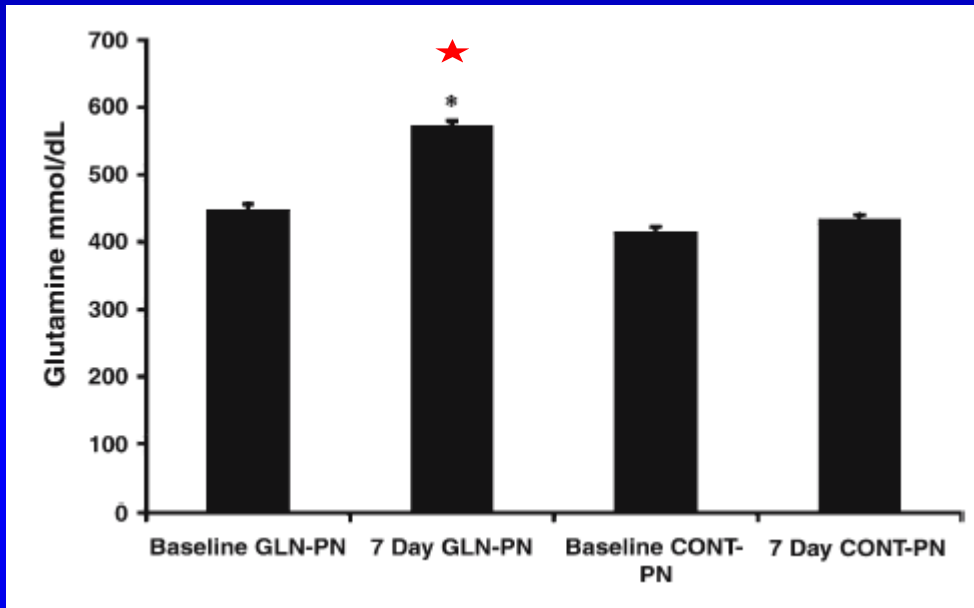
Estívariz CF, Griffith DP, Ziegler TR. JPEN J Parenter Enteral Nutr. 2008 Jul-Aug;32(4):389-402

- Group 1: isocaloric/isonitrogenous parenteral nutrition, providing 1.5 g/kg/d standard glutamine-free amino acids (STD-PN)
- Group 2 : 1.0 g/kg/d standard amino acids + 0.5 g/kg/d glutamine dipeptide (GLN-PN)
- **N=59 pts**

Thomas R. Ziegler
Lorraine G. Ogden
Kristen D. Singleton
Menghua Luo
Concepcion Fernandez-Estivariz
Daniel P. Griffith
John R. Galloway
Paul E. Wischmeyer

Parenteral glutamine increases serum heat shock protein 70 in critically ill patients

Intensive Care Med (2005) 31:1079–1086



1. HSP-70 cytoprotective effects, including formation of protein complexes for antigen presentation, stabilizing IC proteins
2. ↑ serum HSP-70 levels - ↓mortality in trauma pts
3. GLN - ↑ serum and tissue HSP-70 expression in septic pts

Open Access

Research

Intravenous glutamine decreases lung and distal organ injury in an experimental model of abdominal sepsis

Gisele P Oliveira¹, Mariana BG Oliveira¹, Raquel S Santos¹, Leticia D Lima¹, Cristina M Dias¹, Alexandre M AB¹ Saber², Walcy R Teodoro², Vera L Capelozzi², Rachel N Gomes³, Patricia T Bozza³, Paolo Pelosi⁴ and Patricia RM Rocco¹

¹Laboratory of Pulmonary Investigation, Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro, Av. Carlos Chagas Filho, s/n, Rio de Janeiro, 21949-902, Brazil

²Department of Pathology, Faculty of Medicine, University of São Paulo, Dr. Arnaldo Street, 455, Sao Paulo, 01246-903, Brazil

³Laboratory of Immunopharmacology, Oswaldo Cruz Institute, FIOCRUZ, Avenida Brasil 4365, Rio de Janeiro, 21045-900, Brazil

⁴Department of Ambient, Health and Safety, University of Insubria, c/o Villa Toeplitz Via G.B. Vico, 46 21100 Varese, Italy

Corresponding author: Patricia RM Rocco, pmrocco@gmail.com

The glutamine story: where are we now?

Paul E. Wischmeyer

Metabolické změny

- Metabolizmus glukózy
- Metabolizmus AMK
- **Metabolizmus MK**

Metabolizmus MK

- Zvýšená hladina FFA
- Cholesterol – pokles hladiny představuje nepříznivý prognostický marker

CAVE:

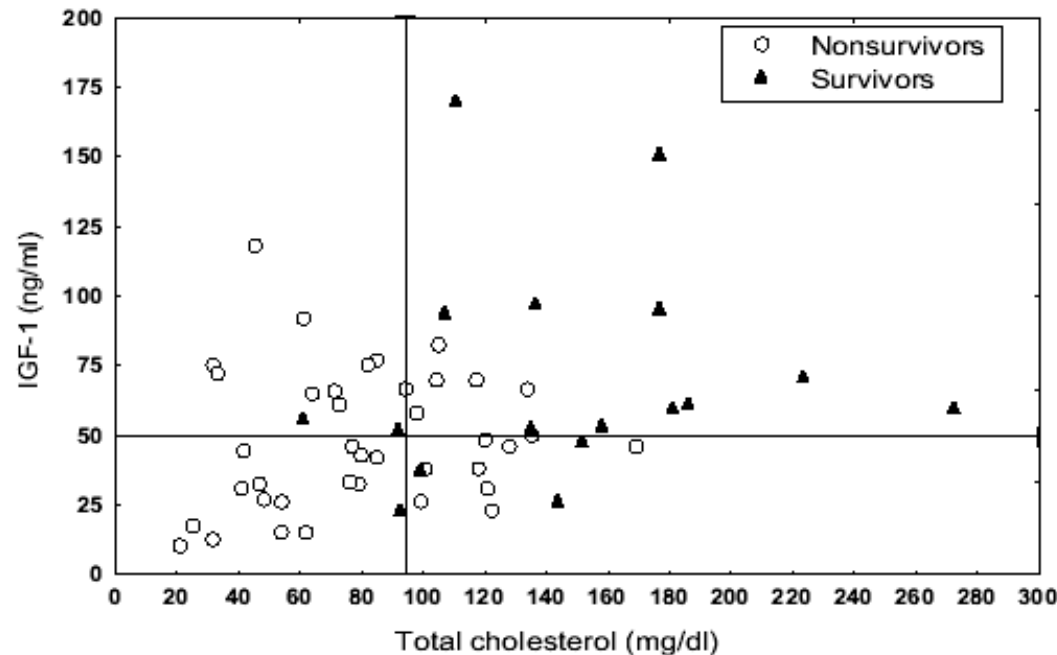
Kontrola glykémie se podílí na korekci dyslipidémie

Nutriční režim s lipidy musí být monitorován

Low insulin-like growth factor-1 and hypocholesterolemia as mortality predictors in acute kidney injury in the intensive care unit*

Crit Care Med 2008 Vol. 36, No. 12

Sérgio M. Guimarães, MD, PhD; Emerson Q. Lima, MD, PhD; José P. Cipullo, MD, PhD; Suzana M. Lobo, MD, PhD; Emmanuel A. Burdmann, MD, PhD



↓ levels of insulin-like GF-1 and cholesterol were clearly related to higher mortality. The close correlation of insulin-like GF-1 with nutritional status, serum stability, and short-half life makes it a suitable candidate for an early and sensitive marker for intensive care unit AKI mortality.

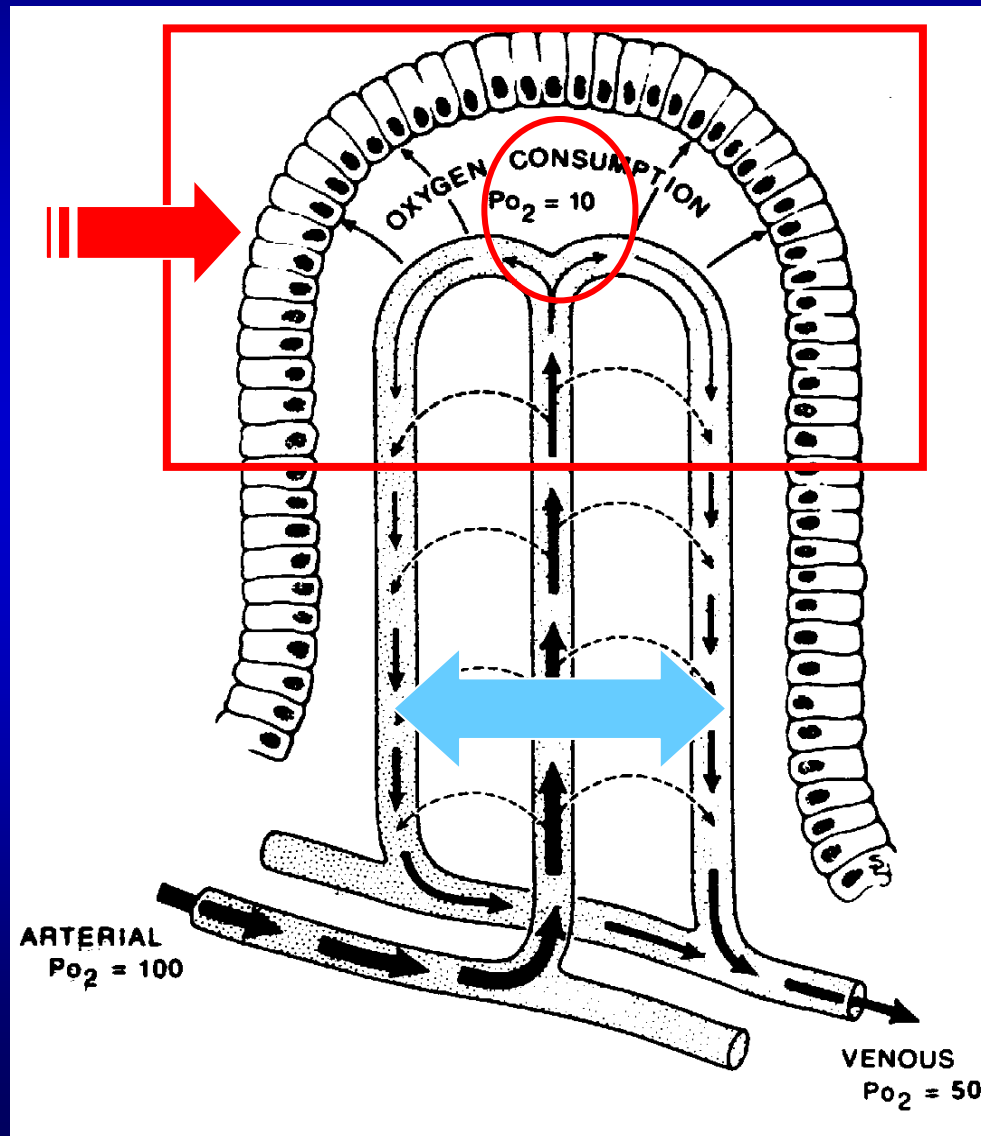
Přirozené bariéry a jejich integrita

- Perfúze – hypoperfúze, I/R trauma
- Substráty – glu a gln
- Oxidační stress - SIRS

- 3 bariéry v přímém kontaktu s okolním prostředím: kůže, plíce, GIT
- GIT – přirozená bariéra s kontaminovaným obsahem (~ 400 bakteriálních a mykotických kmenů)
- Splanchnikus – ↓ SBF při jakémkoli inzultu – stresová odpověď na inzult

Střevní slizniční mikrocirkulace

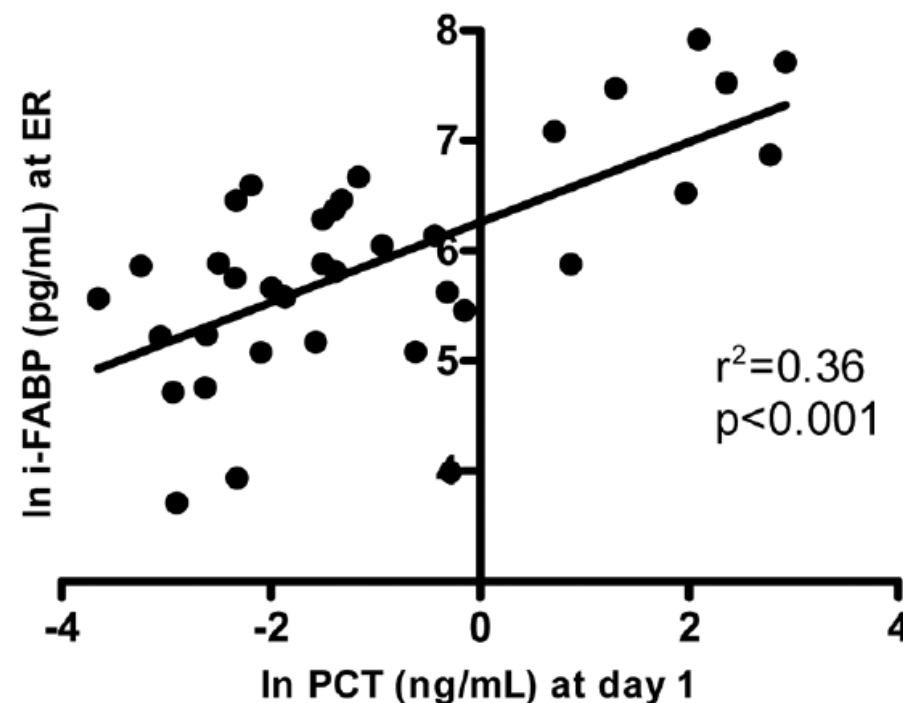
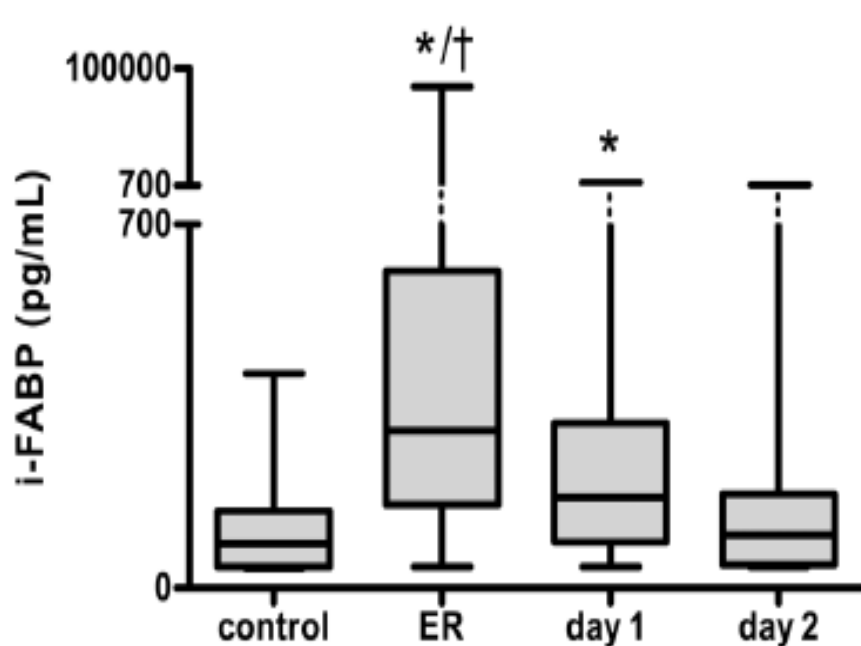
↓ SBF



Rapid development of intestinal cell damage following severe trauma: a prospective observational cohort study

Jacco J de Haan¹, Tim Lubbers¹, Joep P Derikx^{1,2}, Borna Relja³, Dirk Henrich³, Jan-Willem Greve^{4,1}, Ingo Marzi³ and Wim A Buurman¹

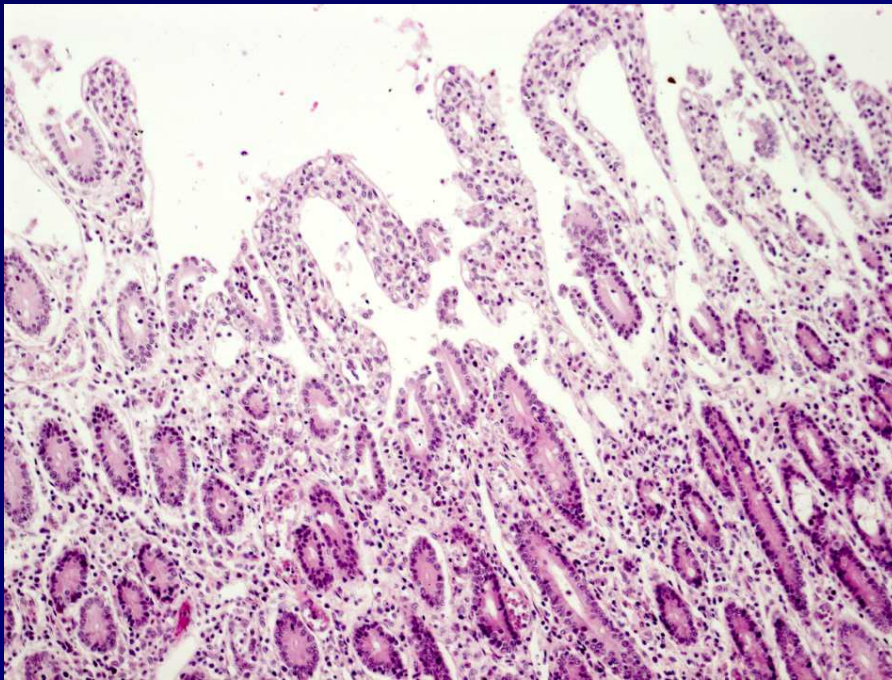
Prospective observational cohort study in 96 adult trauma patients. Upon arrival at the emergency room (ER) plasma levels of i-FABP



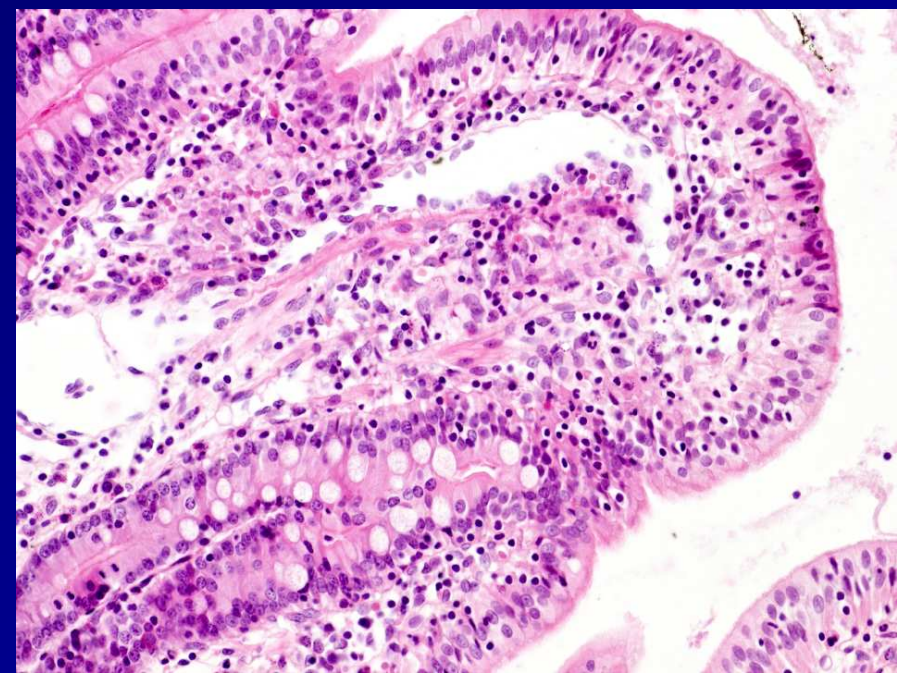
SELECTIVE INDUCIBLE NITRIC OXIDE SYNTHASE INHIBITION DURING LONG-TERM HYPERDYNAMIC PORCINE BACTEREMIA

Martin Matejovic,* Ales Krouzecky,* Vendula Martinkova,* Richard Rokyta, Jr.,
Hana Kralova,‡ Vladislav Treska,§ Peter Radermacher,† and Ivan Novak*

Intestinal histology



Septic shock



Septic shock + L-NIL

SELECTIVE INDUCIBLE NITRIC OXIDE SYNTHASE INHIBITION DURING LONG-TERM HYPERDYNAMIC PORCINE BACTEREMIA

Martin Matejovic,^{*} Ales Krouzecky,^{*} Vendula Martinkova,^{*} Richard Rokyta, Jr.,
Hana Kralova,[‡] Vladislav Treska,[§] Peter Radermacher,[†] and Ivan Novak^{*}

Intestinal histology



**Adekvátní a včas
podaná antimikrobiální
léčba !!!**

Septic shock

Septic shock + L-NIL

Možnosti ovlivnění

- Tekutinová resuscitace a kapilární recruitment
- Kontrola infekce – eliminace vlivu inzultu
- Kontrola homeostázy
 - Kontrola glykémie (NICE –SUGAR 2009)
 - Substituce GLN
 - Zvýšení antioxidační kapacity – NAC, Se, Zn
 - Suplementace vitaminů (ve vodě rozpustných – Thiamin)

Závěr

- Terapeutické priority
- Každé dílčí opatření bez adekvátní léčby obtížně hodnotitelné
- Ovlivnění metabolických změn dle aktuální vývoje stavu vnitřního prostředí
- Cíl: kontrola homeostázy

Děkuji za pozornost !

