Sweet'N Low et. Al
Hyperglycemia'N Nutrition Support
Food Feud: Clinical Pearls for 2004

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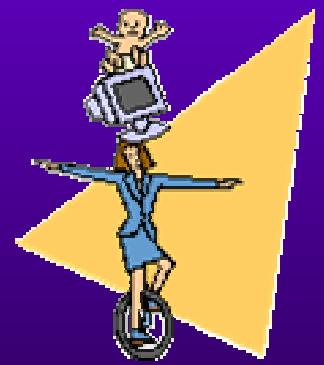
Tuesday February 10, 2004



The Times-Picayune

50 CENTS 166th year No. 347 MONDAY, JANUARY 5, 2004 METRO EDITI

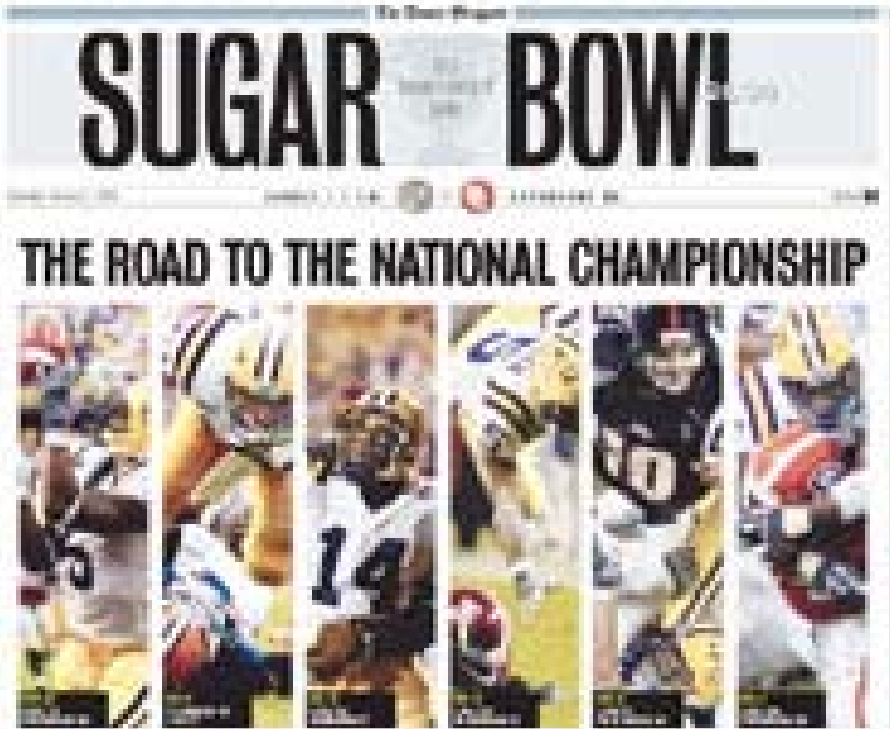
21 TIGERS SOONERS 14

LSU No. 1

SUGAR BOWL VICTORY GIVES TIGERS FIRST TITLE SINCE 1958

STAFF PHOTO BY ALEX BRANDON

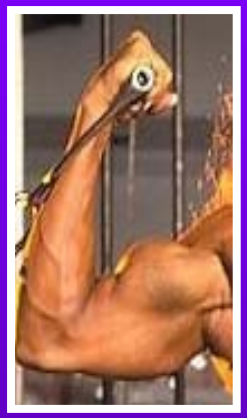
LSU head coach Nick Saban holds the trophy signifying the BCS championship as linebacker Chad Lavalais, left, and wide receiver Michael Clayton, second from left, and other Tiger players cele-

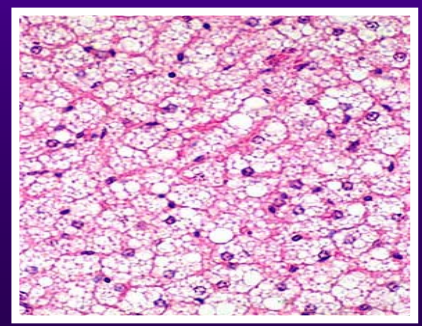


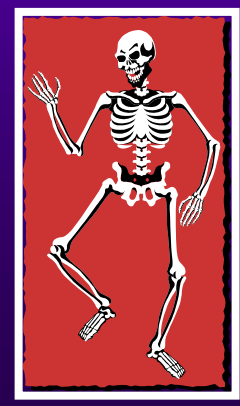
Objectives

- List the benefits of euglycemia (and risks of hyperglycemia)
- Develop an algorithm for the monitoring, prevention and management of hyper- and hypo- glycemia.
- (Laissez Les Bons Temps Rouler!!)

Starvation Vs. Stress







HORMONAL RESPONSE to STARVATION & STRESS

	Acute Starvation	Chronic Starvation	Trauma/ Sepsis I	Sepsis II
INSULIN	-	-	-	++
GLUCAGON	+	N	++	++
CORTICO-STEROIDS	+	+	++	++
GROWTH HORMONE	+	+	+	+
CATECHOL-AMINES	+	N	+++	+++

Stress Hyperglycemia

- a. k. a. "diabetes of stress" or "pseudo-diabetes"
- Associated with increased morbidity and mortality
- Potential enhancement by TPN
- Insulin resistance (peripheral & hepatic)
- Elderly at higher risk

When Sweet Turns "Sour"

- Increased mortality and disability in non-diabetic patients.
- Increased CVC infection rates in diabetic patients. (McMahon)
- Increased mortality from AMI in diabetic patient (Malmberg et. al.)
- Impaired immunologic response to infection (Rayfield et. al.)
- Impaired gastrointestinal motility (Oster-Jorgensen et.al)
- Increased cardiovascular tone (Guigliano et. al.)

Other Potential Detrimental Effects of Hyperglycemia

- Increased incidence of mediastinits in diabetic patients undergoing CABG
- Hyperosmolarity
  - (2Na+Gluc/18+Bun/2.8)
- Osmotic diuresis
- Electrolyte imbalance
- Glycation (glycosylation) of immunoglobulins (Hennessey et. al.)

Hyperglycemia – In Vitro Abnormalities

- Granulocyte adhesion
- Chemotaxis
- Phagocytosis
- Respiratory burst
- Intracellular killing
- Complement function
- Predisposing environment for Candida albicans infection

Hyperglycemia - How sweet it is !

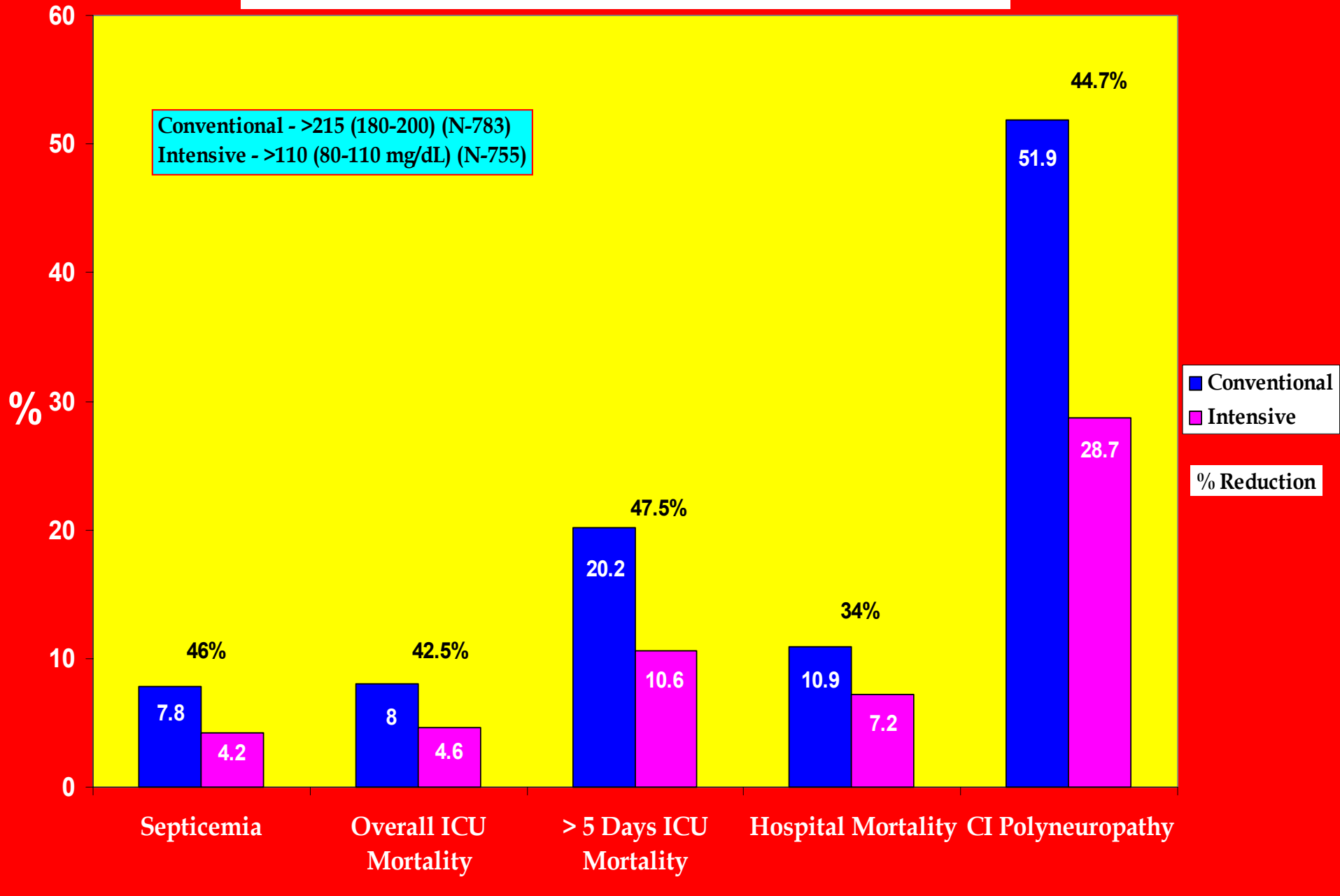
How sweet is sweet?

- 220 mg/dL ?
- 200 mg/dL ?
- 180 mg/dL ?
- 150 mg/dL ?
- 145 mg/dL ?
- 130 mg/dL ?
- 120 mg/dL ?
- 110 mg/dL ?

Hyperglycemia Contributing Factors
Rule of Ds

- Dextrose –PB, TPN, EN, PO liquids
- Diabetes
- Disease (Stress, Insulin resistance)
- Drugs (Steroids, Propofol, vasopressors, et. al.)
- Dialysis – CAPD, CAVHD
- Decreased intravascular volume
- Decreasing youth (aging)
- Doctors et. al.
- Da family , Doughnuts et. al.

Intensive Insulin Therapy In Critically Ill Patients
Van den Berghe et. al. 2001 & 2003



Insulin Vs. Glucose - Hero or Villain?

- Glucose Control And Mortality in Critically Ill Patients. Finney et. al. JAMA 290, 2003
  - End point- ICU mortality
  - Six bands (ranges) of glycemic control
  - Proportion of admission time spent by individual patient in each band was measured
- Conclusions:
  - Increased insulin administration positively associated with ICU death regardless of glucose level
  - Control of glucose level appear to account for mortality benefit
  - Speculative glucose upper limit of 145 mg/dL

Management of Hyperglycemia

- Reduce CHO & Insulin resistance –
  - TPN: <25 kcal/kg/d (total calories) - "permissive underfeeding"
  - Protein 1.2 – 1.5 gm/kg/d
  - Parenteral Willett, Atkins formulas?
- Set goal range (mg/dL)
  - 80-110 Van den Berghe et. al.
  - 80-120 (100-150 if medically stable) McMahon
  - <145 Finney et. al.
- Goal rate
  - <4 mg/kg/min. Begin @ 3mg/kg/min (actual/usual wt.) If > 10% above ideal, use ideal wt. (Rosmarin et. al.)

Management of Hyperglycemia

- Remember: The lower the maximum goal level, the greater the risk of hypoglycemia.
- Infuse *low* and *slow* and increase according to monitored glucose levels.
- Minnie (Sweet) Pearls(@ Glucose):
  - 1 mmol =180 mg
  - To convert mmol/L to mg/dl, multiply by 18
  - To convert mg/dL to mmol/L, multiply by 0.05551

Sliding - Sliding Scales

Glucose	Ins	Ins	Glucose	Ins
<150	0		<100	0
150-200	5		100-150	2
201-250	10	5	151-200	4
251-300	15	10	201-250	6
301-350	20	15	251-300	8
351-400	25	MD	>300	10
401-450	30			
>451	MD			

Insulin in TPN Solution

- Plasma glucose level reasonably controlled < 200 mg/dL
- Influencing factors controlled
- Dose not requiring change < 24 hr.
- Administration dose:
  - 0.1 IU/gm CHO/L
  - Increase by 0.05 IU/gm CHO/L until glucose controlled.

Insulin Infusions
Multiple Protocols

- 1 IU/ml in NaCl
- Limited to ICU or closely monitored units
- Frequent glucose determinations & rate adjustment – q. 1 hr. initially
- 1-2 IU/hr. initially, titrated according to established protocols and ranges of glucose levels

Insulin Infusions
Multiple Protocols

- Mirtallo –
  - 2 IU/hr. Initiate @>180mg/dL Adjusted until <200 mg/dL, limit<15 IU/hr.
- Van den Berghe et. al. -
  - "Strict algorithm". Initiate @>110mg/dL, limit 50 IU/hr.
- Mizock - Brown & Dodek -
  - 3 IU bolus + 2 IU/hr. @>207 mg/dL
  - Comprehensive nomogram – no limit
- Monitor, monitor, monitor

Browm G and Dodeck P, Intravenous insulin nomogram improves blood glucose control in critically ill patients, Critical Care Medicine, 2001; 29:1714-1719.

Mizock BA G, Glucose Control in the ICU, Nutrition & the M.D. 2003; 29(11):1-4.

INSULIN INFUSION PROTOCOL - Regular Human Insulin Only (ICU only)

GOAL: The goal is to maintain serum glucose between 7 and 11.5 mmol/L

MONITORING: Check glucose **q1h** (either capillary or blood) until stable **(3 values in desired range)**. Checks can be reduced to q2h x 4 hours → q4h if blood glucose remains in desired range. Restart q1h checking if any change in insulin infusion rate occurs. If glucose is changing rapidly (even if in the desired range) **OR** if in a critical range (<3.5 or >20mmol/L) q30minute checks may be needed. However, blood glucose will not change significantly in <30 minutes with any change in insulin.

Initiating Insulin Infusion

Glucose	11.5-14mmol/L	14.1-17mmol/L	17.1-20mmol/L	20.1-24mmol/L	>24mmol/L
	Give 3 units insulin IVP and start @ 2 units/hr	Give 6 units insulin IVP and start @ 2 units/hr	Give 8 units insulin IVP and start @ 2 units/hr	Give 10 units insulin IVP and start @ 2 units/hr	Call MD for orders

Ongoing Insulin Infusion:

Below Desired Range (7-11.5mmol/L)

Glucose Level	Infusion Rate of 1-3 units/hr	Infusion Rate of 4-6 units/hr	Infusion Rate of 7-9 units/hr	Infusion Rate of 10-12 units/hr	Infusion Rate of 13-16 units/hr	Infusion Rate of > 16 units/hr
< 3.5mmol/L	D/C Infusion and give 1 amp D50 IVP					
3.5-4.5mmol/L	D/C Infusion: Re-check glucose in 1 hour. If >7, re-start but decrease rate by 1unit/hr.		D/C Infusion: Re-check glucose in 1 hour. If >7, re-start but decrease rate by 2 unit/hr.		D/C Infusion: Re-check glucose in 1 hour, If >7, re-start but decrease rate by 3 unit/hr.	
4.6-5.5mmol/L	D/C Infusion: Re-check glucose in 1 hour, if > 7, re-start but decrease rate by 1 unit/hr.	Decrease Infusion by 50%				
5.6-7mmol/L	Decrease Infusion by 1 unit/hr	Decrease Infusion by 2 units/hr	Decrease Infusion by 3 units/hr	Decrease Infusion by 4 units/ hr	Decrease Infusion by 5 units/hr	Decrease Infusion by 6 units/hr

In Desired Range (7-11.5mmol/L)

7-11.5mmol/L	**NO CHANGES NOW** If glucose continues to decrease within the desired range over 3 consecutive hours, decrease rate by 1 unit/hr.	**NO CHANGES NOW** If glucose continues to decrease within the desired range over 3 consecutive hours, decrease rate by 2 unit/hr..

Above Desired Range (7-11.5mmol/L)

Glucose Level	Infusion Rate of 1-5 units/hr	Infusion Rate of 6-10 units/hr	Infusion Rate of 11-16 units/hr	Infusion Rate of > 16 units/hr
11.5-14mmol/L	Give 2 units insulin IVP and increase Infusion by 1 unit/hr	Give 3 units insulin IVP and increase Infusion by 2 units/hr	Give 3 units insulin IVP and increase Infusion by 3 units/hr	Call Physician for New Order
14.1-17mmol/L	Give 3 units insulin IVP and increase Infusion by 1 unit/hr	Give 5 units insulin IVP and increase Infusion by 2 units/hr	Give 5 units insulin IVP and increase Infusion by 3 units/hr	
17.1-20mmol/L	Give 8 units insulin IVP and increase Infusion by 1 unit/hr	Give 8 units insulin IVP and increase Infusion by 2 units/hr	Give 8 units insulin IVP and increase Infusion by 3 units/hr	
20.1-24mmol/L	Give 10 units insulin IVP and increase Infusion by 1 unit/hr	Give 10 units insulin IVP and increase Infusion by 2 units/hr	Give 10 units insulin IVP and increase Infusion by 3 units/hr	
> 24mmol/L	Call Physician for New Order			

Management of Hypoglycemia

- Varied definitions < 60mg/dL, Sx?
- Dextrose 50% IVP
  - 25 – 50 ml ½ - 1 amp
  - 12.5 - 25 gm
- Glucagon (Subcutaneous, IM or IV)
  - 0.5 - 1 mg repeat in 20 min if needed
  - Self-injectors available
- Oral
  - O. J., glucose tabs, et. al.
  - Sublingual sugar

Pearls, Aphorisms & Lagniappe

- If a little is good, a lot is not necessarily better
- Halitosis is better than no breath at all.
- The enemy of good is better.
- When at first you don't succeed, consult.
- The ignorance of facts does not make them disappear.
- Man who looks at leopard through bamboo pole sees only one spot.

Pearls, Aphorisms & Lagniappe

- Often the therapy is worse than the disease.
- Primum non noncere.
- When you are up to part of your anatomy in alligators, it is hard to remember that your primary purpose was to drain the swamp.
- Illegitimi non carborundum.
- NCP June 2004 Issue "Enhancing Response to NS in Critical Patients" Invited review article: "Hyperglycemia and Nutrition Support: Theory and Practice" McCowen & Bistrian (a.ka. et. al.)
- Nutrition Week 2004 - Practice Posters N44, 63, 65

A.S.P.E.N. Rhoads Research Foundation Request for Proposals

- **Intensive Glycemic Control in Critically Ill Patients Receiving TPN**
- **Purpose**
  - The principal objective of this request is to support meritorious hypothesis-driven clinical research that examines the role of intensive glucose management in critically ill patients receiving total parenteral nutrition (TPN).

http://www.nutritioncare.org/research/rpf_03.pdf

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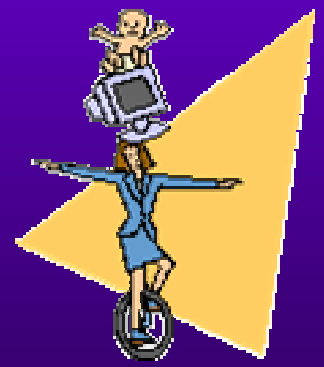

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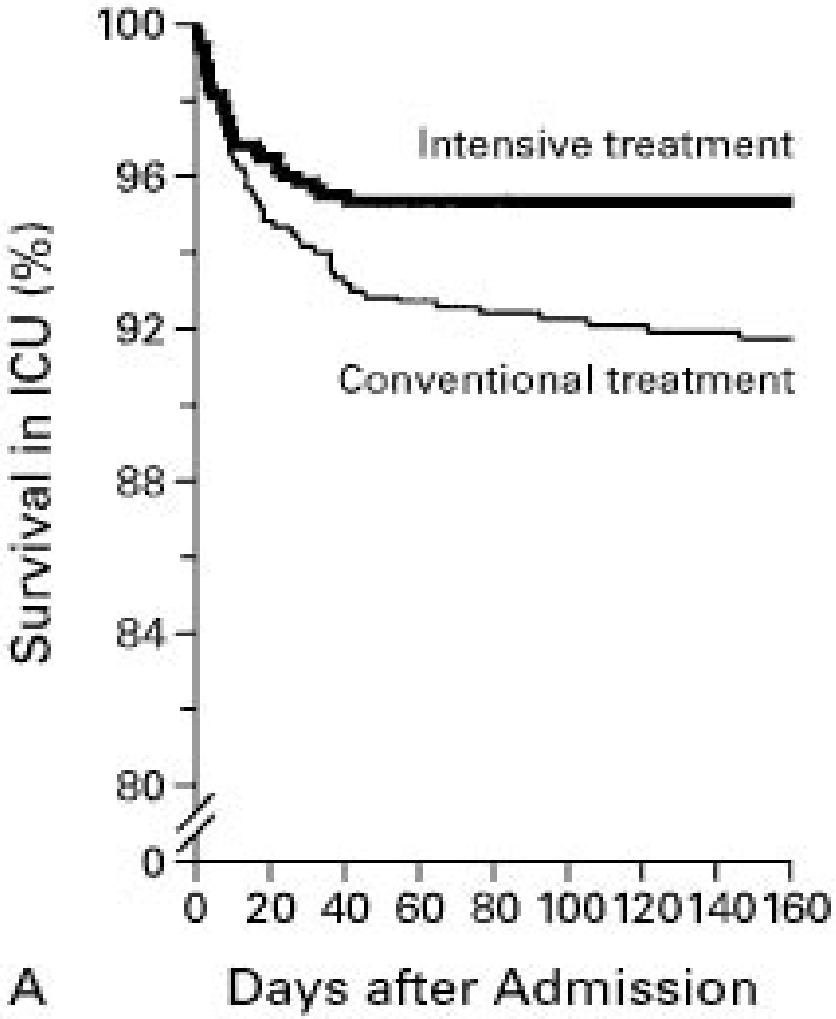
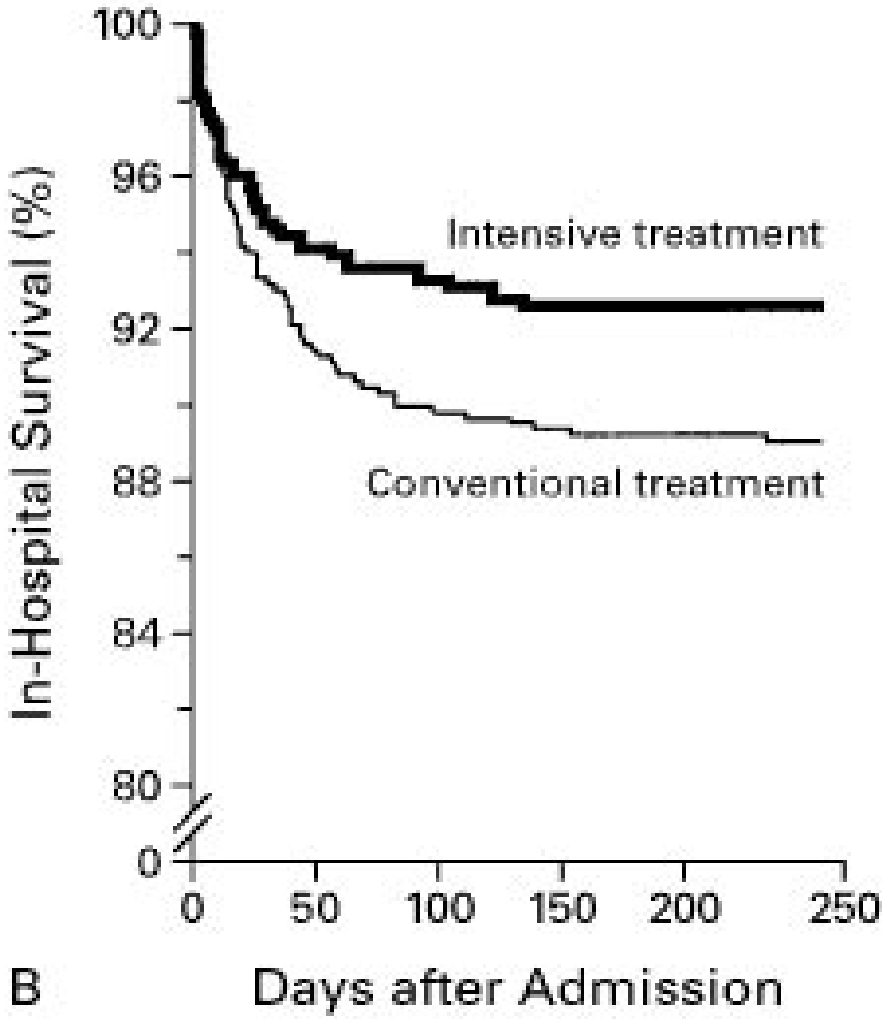
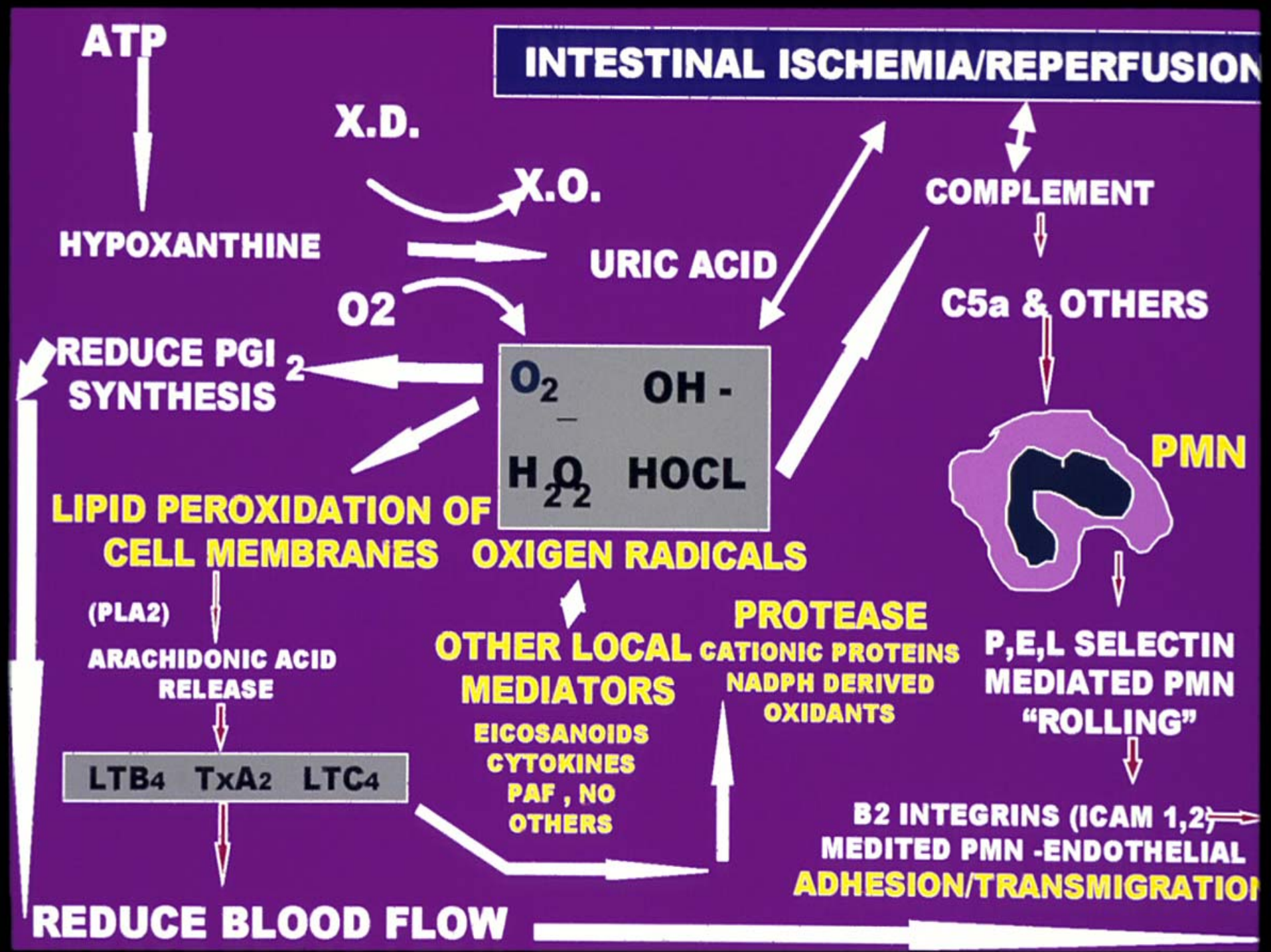
American Society for Parenteral and Enteral Nutrition
ASPEN

Kaplan-Meier Curves Showing Cumulative Survival of Patients Who Received Intensive Insulin Treatment or Conventional Treatment in the Intensive Care Unit (ICU)





Van den Berghe, G. et. al. N Engl J Med 2001;345:1359-1367


ATP
INTESTINAL ISCHEMIA/REPERFUSION
X.D.
X.O.
COMPLEMENT
HYPOXANTHINE
URIC ACID
O2
C5a & OTHERS
REDUCE PGI2 SYNTHESIS
O2 OH -
H2O2 HOCL
PMN
LIPID PEROXIDATION OF CELL MEMBRANES
OXIGEN RADICALS
(PLA2)
ARACHIDONIC ACID RELEASE
OTHER LOCAL MEDIATORS
EICOSANOIDS
CYTOKINES
PAF , NO
OTHERS
PROTEASE
CATIONIC PROTEINS
NADPH DERIVED OXIDANTS
P,E,L SELECTIN MEDIATED PMN "ROLLING"
LTB4 TxA2 LTC4
B2 INTEGRINS (ICAM 1,2) MEDITED PMN -ENDOTHELIAL ADHESION/TRANSMIGRATION
REDUCE BLOOD FLOW