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Pancreatitis: Critical care and Nutritional Considerations

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No disclosures

Pathophysiology

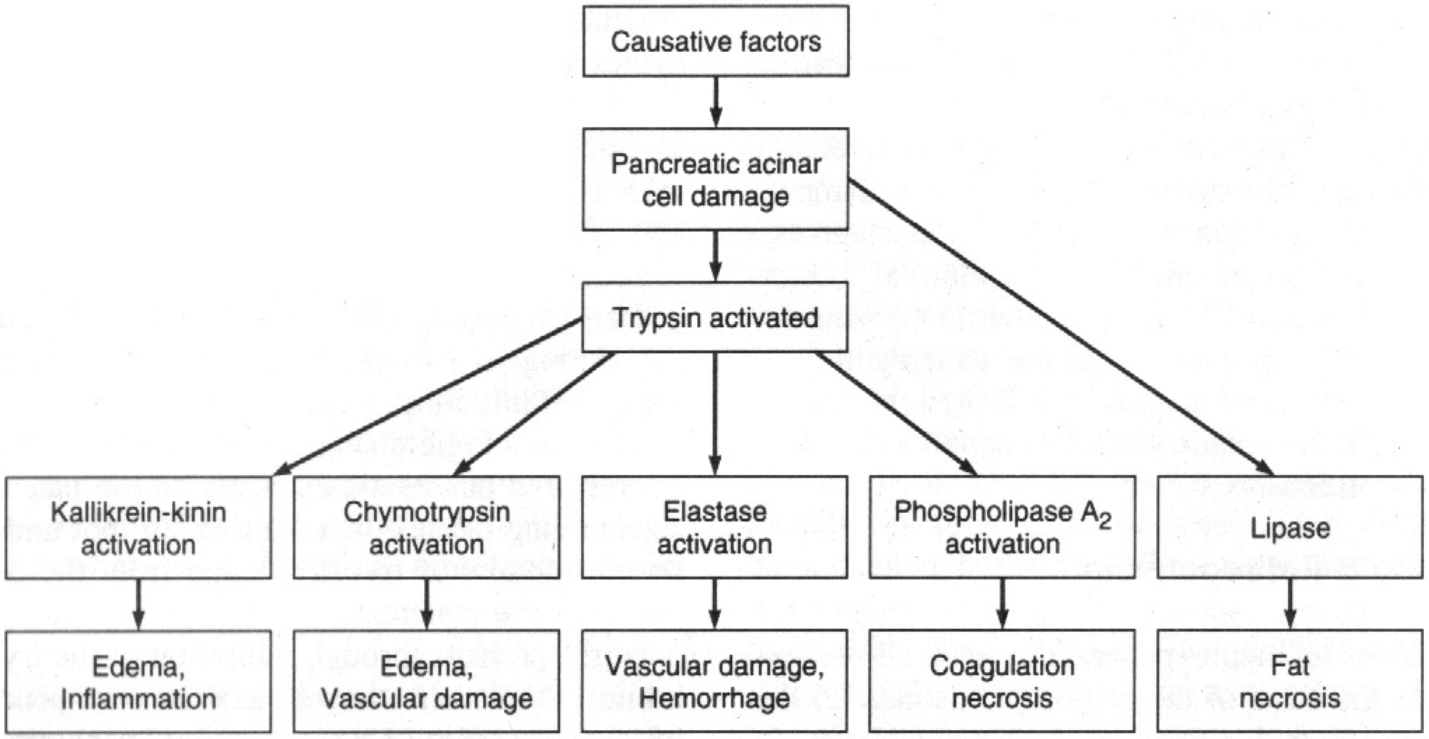
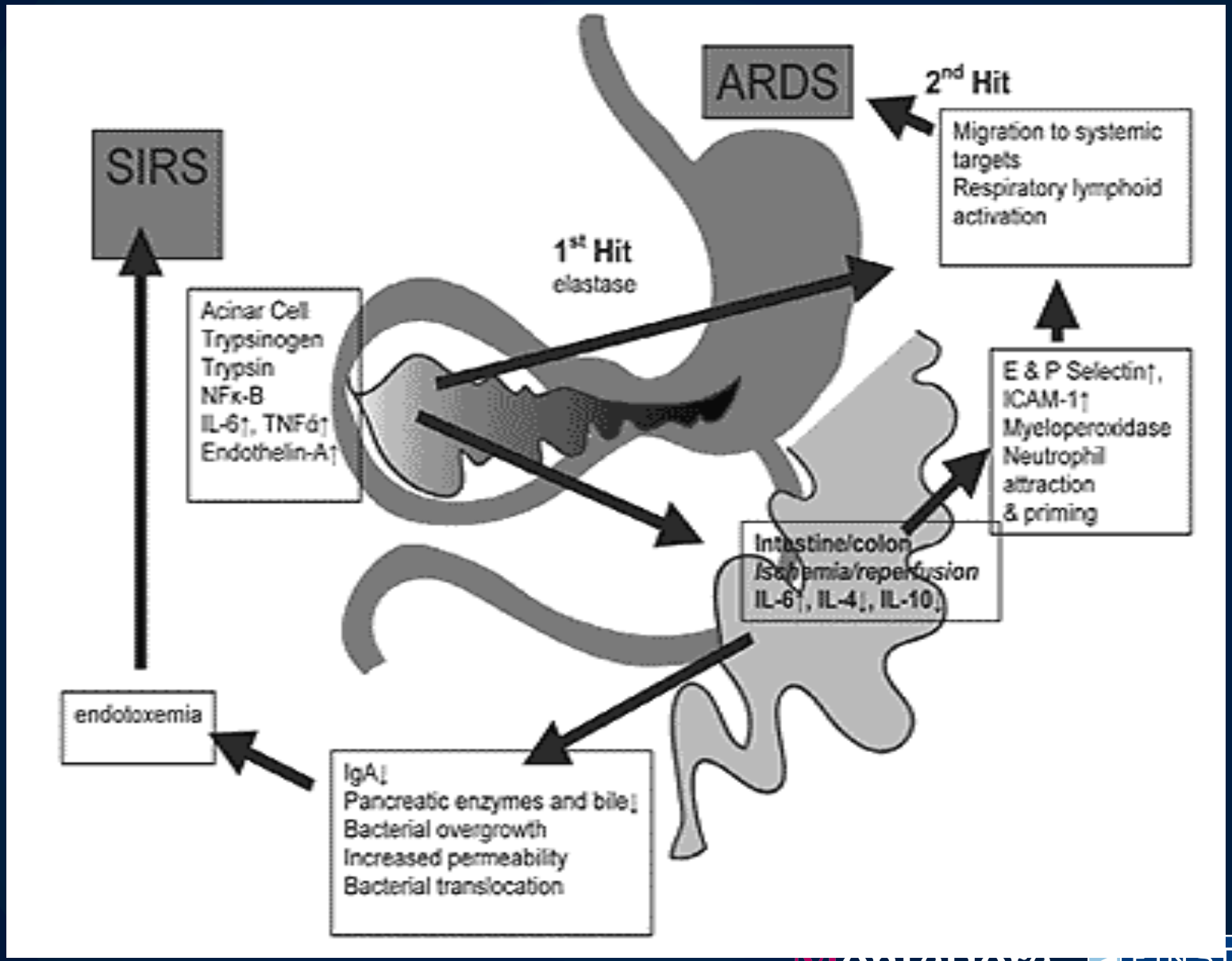


Figure 15–3. Hypothesized pathogenesis of acute pancreatitis. (Reproduced with permission from Marshall JB: Acute pancreatitis: A review with an emphasis on new developments. Arch Intern Med 1993;153:1185.)



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Mr. H.

42 yo male found to have gallstone pancreatitis

- APACHE: 8
- HCT: 44
- Organ dysfunction
  - Lactate 2.3, normal kidneys, on room air
- Hemodynamics
  - Normal BP, no tachycardia, afebrile
- Pulmonary Status
  - Breathing comfortably on room air,
  - CXR: small left pleural effusion

Would you admit Mr. H to the ICU????

Morning after admission – s/p 8L fluid – now hemoconcentrated to HCT 49, lactate increased to 4.9 and decrease urine output

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Need for ICU…..

- For assessment of individual severity there are several factors that should trigger admission/need for transfer to ICU:
  - APACHE II
  - HCT elevation (>44) not responsive to therapy
  - Older age
  - Obesity
  - Pleural effusion / infiltrate on CXR
  - Evidence or organ failure
- Ransom's score
- SOFA score
- CT Severity Index

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CT Severity Index

FINDINGS	POINTS
Normal pancreas	0
Gland enlargement	1
Peripanc inflammation	2
1 fluid collection	3
> 1 fluid collection	4
< 30% Necrosis	2
30 – 50% Necrosis	4
>50% Necrosis	6
Max Total	10

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CTSI: Outcome Predictor

- *Retrospective review 268 patient with both pancreatitis and CT scan*
- *CTSI significantly correlated with all measured outcomes*
- *CTSI > 5 (some fluid and some necrosis) associated with:*
  - *8 X as likely to die*
  - *17 X as likely to have LOS >20 days*
  - *10 X as likely to have debridement*

Simchuk, Am J Surg 2000

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Critical Care Management

- *Fluid resuscitation*
  - *Colloid*
  - *Crystalloid*
  - *Hypertonic saline*
- *Invasive monitoring*
- *Cardiopulmonary support*
- *Nutrition therapy*
  - *Enteral/Parenteral Nutrition*
  - *Timing of initiating feeds*
  - *NG vs NJ feeds*

Colloid versus Crystalloid

- Colloid (Albumin, Hetastarch, Dextran)
  - Volume expansion
  - Maintaining intravascular volume
  - Remain intraluminal
  - Intravascular volume overload, hyperoncotic renal impairment, coagulopathy and anaphylaxis
- Crystalloid, hypertonic saline
  - Distributed in both plasma and interstitial compartments
  - Pulmonary edema, CPM

Aggressive vs Controlled Fluid Hydration

- *Mayo Clinic Group*
  - *Defined aggressive resuscitation*
  - *≥ 33% of volume in 72 hours, given in 24 hours*

Primary Outcomes			
Clinical Outcomes	**Early Resuscitation**	**Late Resuscitation**	**P-value**
Mortality	0	5 (18)	< 0.033
Persistent organ failure	6 (35)	12 (43)	0.309
Mean, DOS, days	40 +/-66	37 +/-70	0.880
Median, DOS, days	12	11	

Gardner et al. Pancreatology 2009;9:770-6

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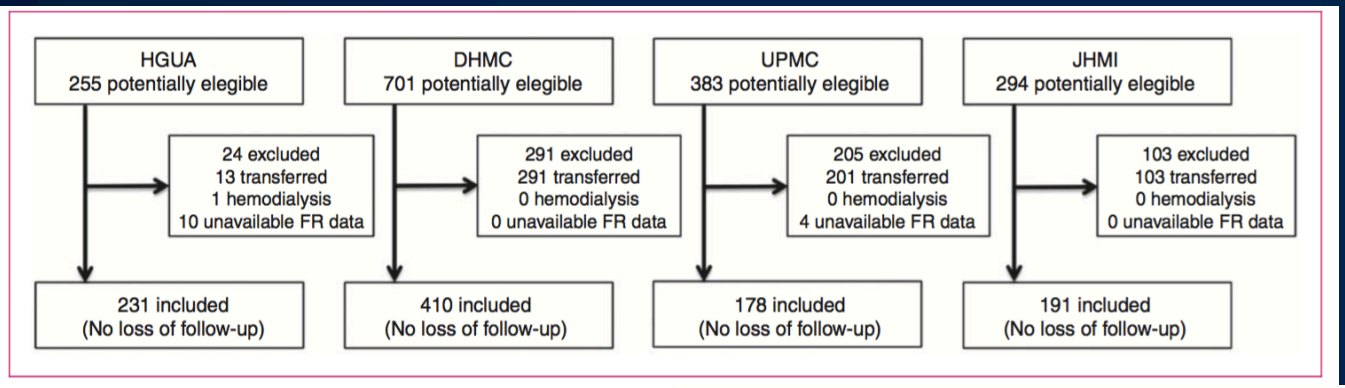
Fluid Resuscitation



1010 patients divided into 3 resuscitation groups:

Nonaggressive < 500 ml
Moderate 500 to 1000 ml
Aggressive > 1000 m

FVER	Local complications	Persistent organ failure	Invasive treatment	Death
<500 ml				
Cases	51/269 (19%)	19/269 (7.1%)	13/269 (4.8%)	8/269 (3%)
OR (95% CI)	*1*	*1*	*1*	*1*
ORa (95% CI)	*1*	*1*	*1*	*1*
500–1000 ml				
Cases	48/427 (11.2%)	19/427 (4.4%)	7/427 (1.6%)	7/427 (1.6%)
OR (95% CI)	0.54 (0.35–0.83)[a]	0.61 (0.32–1.18)	0.33 (0.13–0.83)[a]	0.54 (0.2–1.52)
ORa (95% CI)	0.67 (0.43–1.05)	0.56 (0.28–1.14)	0.37 (0.14–0.98)[b]	0.46 (0.15–1.38)
>1000 ml				
Cases	50/314 (15.9%)	15/314 (4.8%)	5/314 (1.6%)	8/314 (2.5%)
OR (95% CI)	0.81 (0.53–1.24)	0.66 (0.33–1.33)	0.32 (0.11–0.91)[b]	0.85 (0.32–2.3)
ORa (95% CI)	1.15 (0.71–1.86)	0.5 (0.22–1.12)	0.21 (0.05–0.84)[a]	0.64 (0.20–2)

Singh et al. United Euro Gastroenterol. 2017:5(4)491-498

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Nutritional Considerations in Acute Severe Pancreatitis:

Enteral vs Parenteral

Early vs Delayed Enteral Nutrition

Nasogastric vs Nasojejunal Feeds

Early Oral Diet

Immunonutrition: Glutamine supp, Omega fatty acids

Nutrition Support: EN vs PN

- ***Improved outcomes*** *demonstrated with EN in severe pancreatitis*
- *3 meta-analyses of EN vs PN randomized trials:*
  - ⇓ *infectious morbidity (RR=0.46, P = .001)*
  - ⇓ *hospital length of stay (P < .0001)*
  - ⇓ *need for surgical intervention (RR= 0.48)*
  - ⇓ *multi-organ failure*
  - ⇓ *mortality (OR=0.095-0.666; P = .005)*

McClave et al., JPEN, 2006;30:143; Marik, BMJ, 2004;328:1407; Cao et al., Ann Nutr Metab, 2008;53:268

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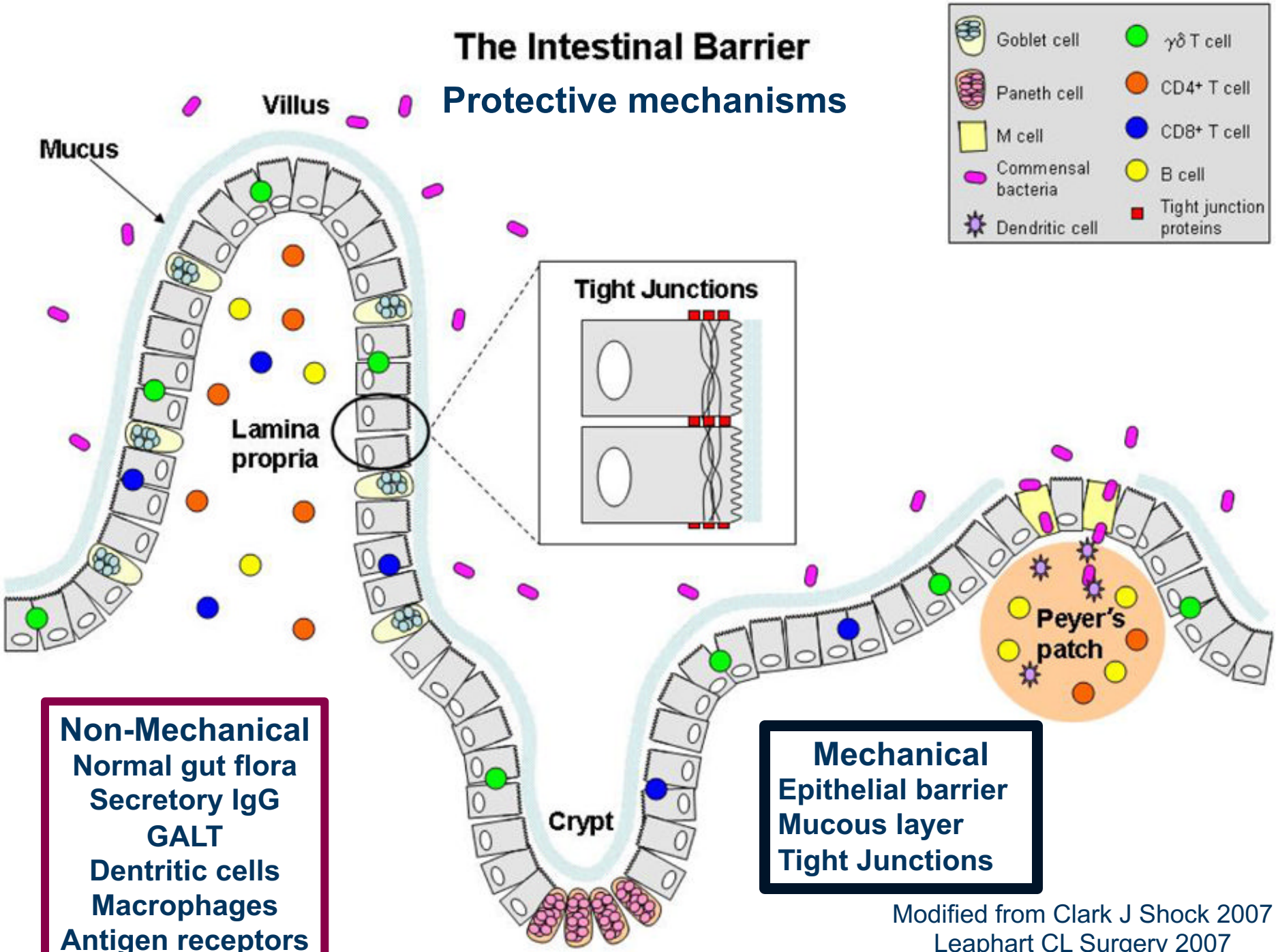
The Intestinal Barrier

Protective mechanisms

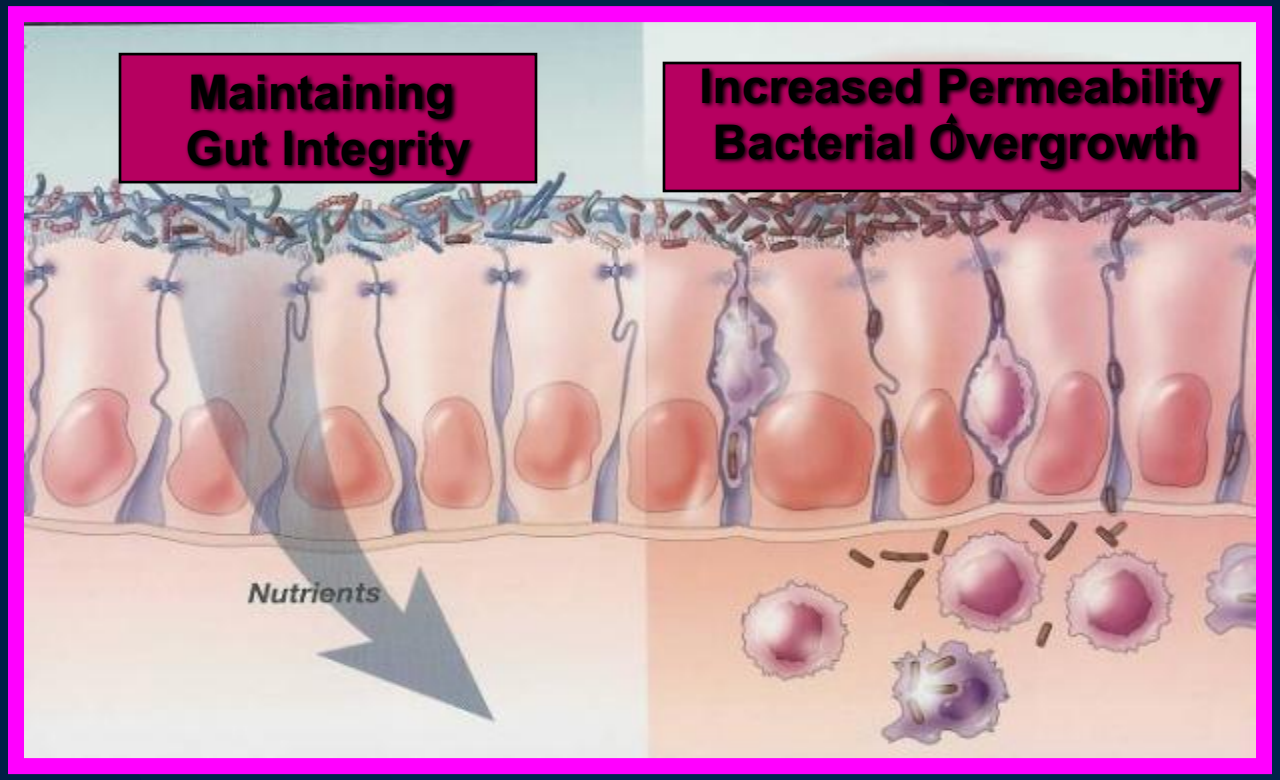


Non-Mechanical
Normal gut flora
Secretory IgG
GALT
Dentritic cells
Macrophages
Antigen receptors

Mechanical
Epithelial barrier
Mucous layer
Tight Junctions

Modified from Clark J Shock 2007
Leaphart CL Surgery 2007

Gut Integrity



Early EN maintains gut integrity, prevents bacterial overgrowth

- Increased gut permeability linked to MOF and disease severity [1]
- Bacterial translocation to MLNs, peritoneum, blood in sepsis [2]
- Sepsis dose Pseudomonas, Staph, E Coli : gut << IV [3]

[1] Ammori (J Gastrointest Surg 1999;3:252)
[2] Ljungqvist (J Trauma 2000;48:314)
[3] Alverdy (J Leuko Biol 2008:83:461)

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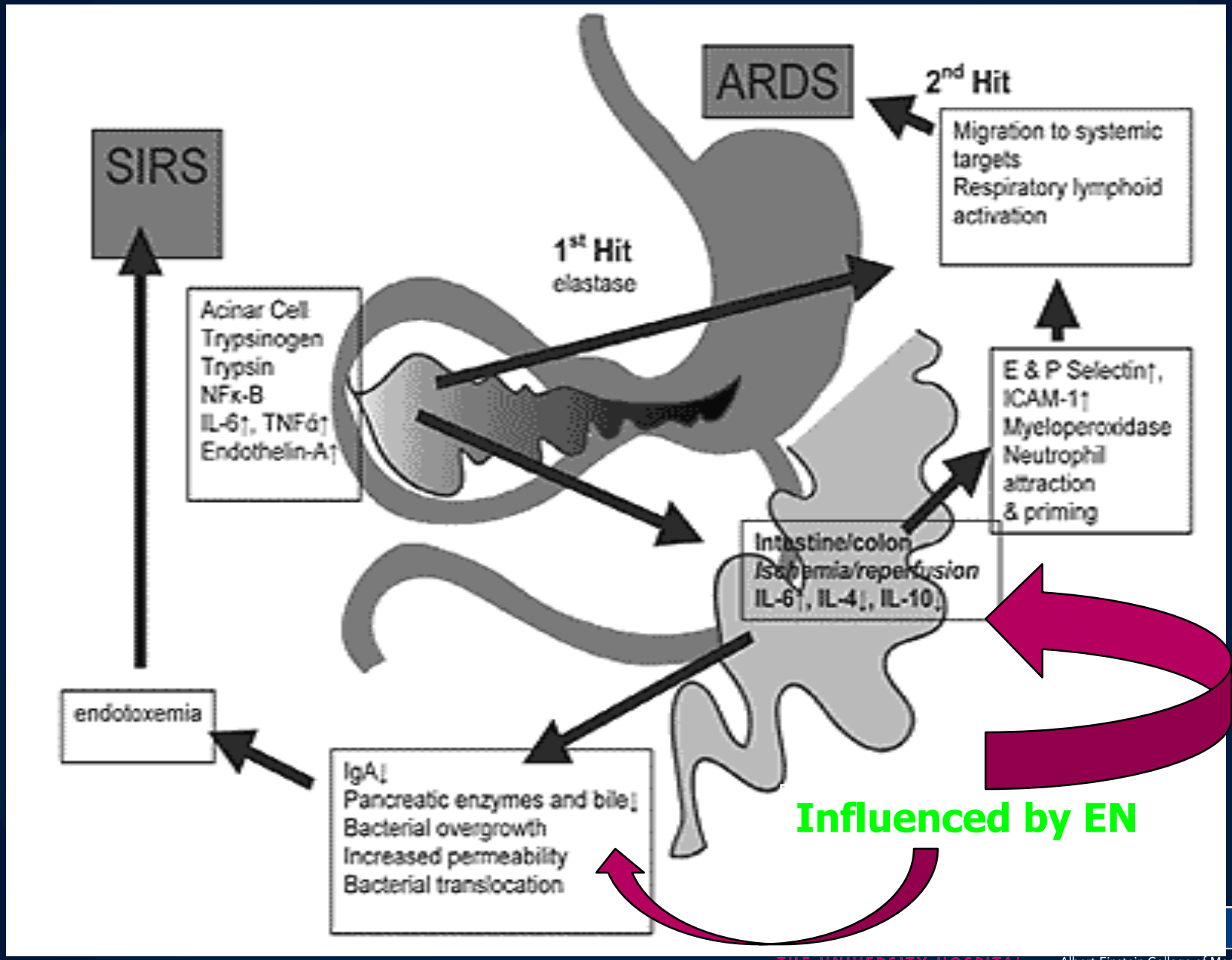
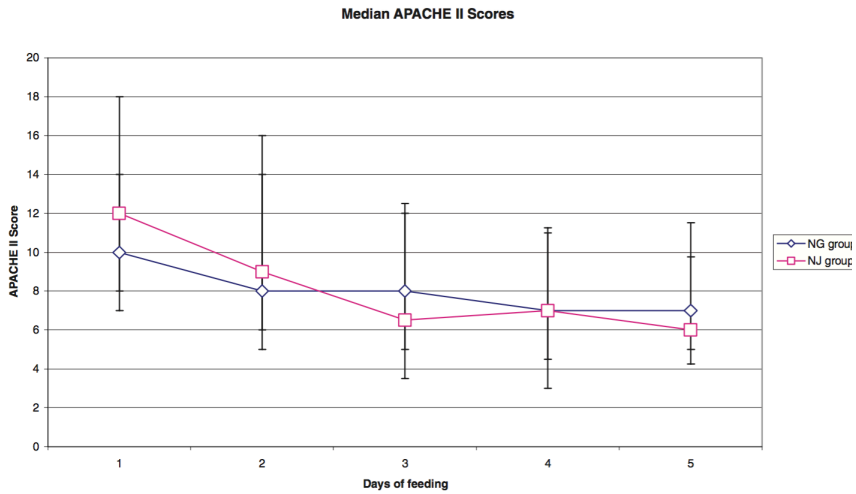
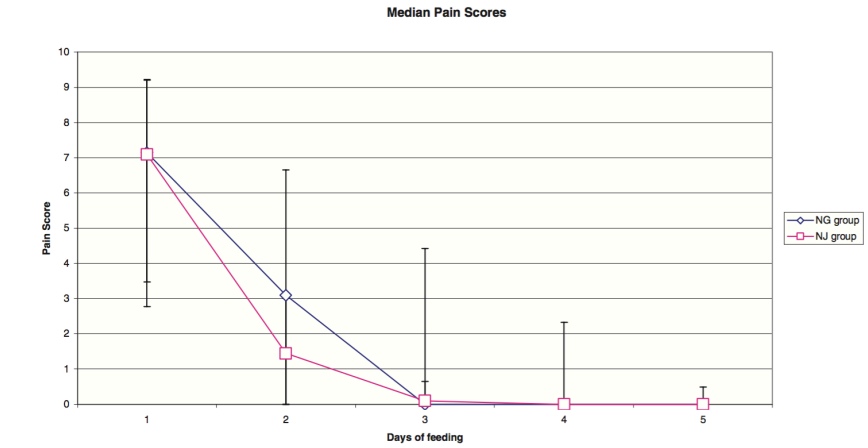
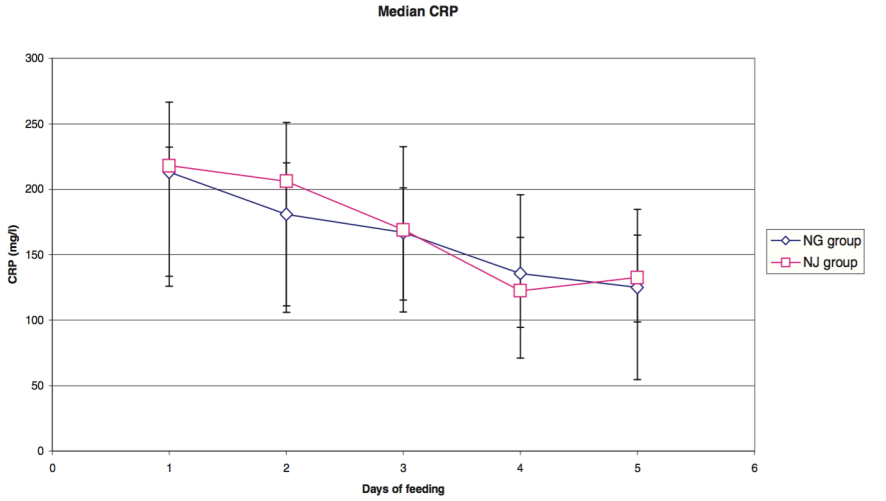

ARDS
2nd Hit
Migration to systemic targets
Respiratory lymphoid activation
SIRS
1st Hit
elastase
Acinar Cell
Trypsinogen
Trypsin
NFκ-B
IL-6↑, TNFα↑
Endothelin-A↑
E & P Selectin↑,
ICAM-1↑
Myeloperoxidase
Neutrophil attraction & priming
Intestine/colon
Ischemia/reperfusion
IL-6↑, IL-4↓, IL-10↓
endotoxemia
IgA↓
Pancreatic enzymes and bile↓
Bacterial overgrowth
Increased permeability
Bacterial translocation
Influenced by EN

A Randomized Study of Early Nasogastric *versus* Nasojejunal Feeding in Severe Acute Pancreatitis

F. C. Eatock, M.D., F.R.C.S., P. Chong, M.B., Ch.B., F.R.C.S., N. Menezes, M.B., Ch.B., F.R.C.S., L. Murray, B.Sc., C. J. McKay, M.D., F.R.C.S., C. R. Carter, M.D., F.R.C.S., and C. W. Imrie, M.B., Ch.B., B.Sc., F.R.C.S.
Lister Department of Surgery and Department of Nutrition and Dietetics, Glasgow Royal Infirmary, Alexandra Parade, Glasgow, Scotland







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NG vs NJ Tube?

- *2 PRCT and 1 meta-analysis: ∅ differences in outcomes*
- *Success = early initiation of support (36-48 hrs of admit)*
- *Minimize degree of ileus*
- *Associated with 92% tolerance*

Jiang K et al., World J Gastroenterol ,2007; 13:5253
Eatock et al., Am J Gastroenterol, 2005;100:432
Kumar et al. J Clin Gastroenterol, 2006;40:431

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early versus On-Demand Nasoenteric Tube Feeding in Acute Pancreatitis

- *Multi-center RCT comparing naso-enteric feeds with oral diet at 72 hours after presentation*
  - *APACHE II ≥ 8*
  - *CRP > 150 mg/L*
- *208 patients*
- *Primary end point*
  - *Composite of major infection*
  - *Mortality during 6 month follow up*

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Bakker et al. N Engl J Med 2014;371:1983-93.

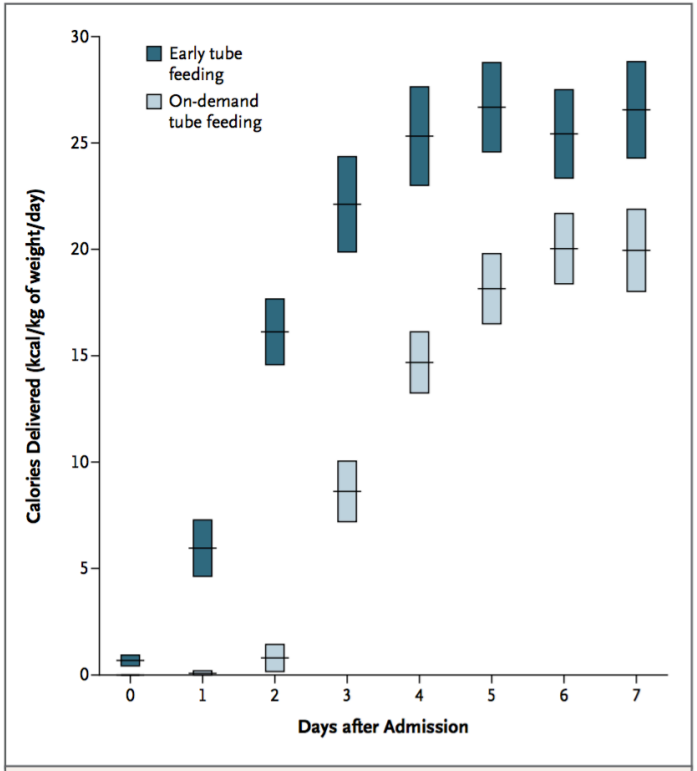

Figure 1. Calories Delivered with the Use of Early versus On-Demand Naso-enteric Tube Feeding.

Each rectangle shows the mean value (horizontal line) and 95% confidence interval (top and bottom of the rectangle).

Table 2. Primary and Secondary End Points, According to the Intention-to-Treat Analysis.*

Outcome	Early Tube Feeding (N=101)	On-Demand Tube Feeding (N=104)	Risk Ratio (95% CI)	P Value
Primary composite end point: infection or death — no. (%)	30 (30)	28 (27)	1.07 (0.79–1.44)	0.76
Secondary end points				
Infection — no. (%)†	25 (25)	27 (26)	0.97 (0.70–1.34)	0.87
Infected pancreatic necrosis	9 (9)	15 (14)	0.74 (0.43–1.26)	0.28
Bacteremia	17 (17)	18 (17)	0.98 (0.68–1.43)	1.00
Pneumonia	12 (12)	13 (12)	0.97 (0.63–1.50)	1.00
Death — no. (%)	11 (11)	7 (7)	1.27 (0.85–1.89)	0.33
Necrotizing pancreatitis — no. (%)‡	64 (63)	65 (62)	1.06 (0.77–1.47)	0.76
CT severity index§	4±2	4±3	—	0.29
ICU admission after randomization — no. (%)	18 (18)	20 (19)	0.95 (0.66–1.38)	0.86
Mechanical ventilation — no. (%)	12 (12)	14 (13)	0.93 (0.60–1.44)	0.84
New-onset organ failure — no./total no. at risk (%)¶				
Single organ failure	26/67 (39)	31/73 (42)	0.92 (0.65–1.32)	0.73
Persistent single organ failure	10/67 (15)	10/73 (14)	1.05 (0.65–1.70)	1.00
Multiple organ failure	7/67 (10)	6/73 (8)	1.14 (0.67–1.95)	0.77
Persistent multiple organ failure	4/67 (6)	4/73 (5)	1.05 (0.51–2.14)	1.00

Bakker et al. N Engl J Med 2014;371:1983-93.

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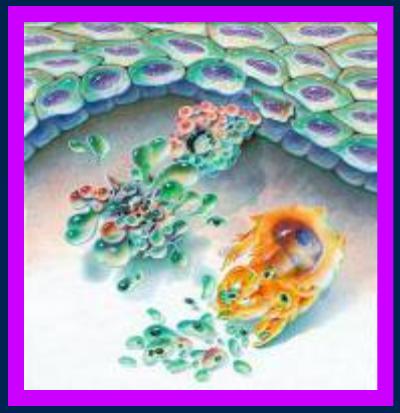
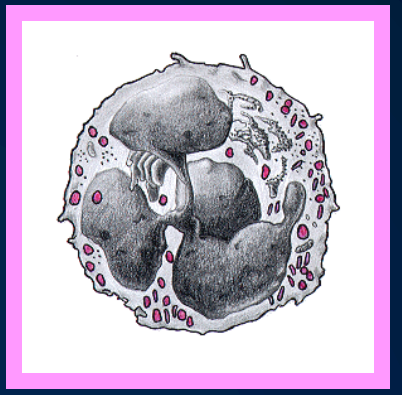
Formula Considerations

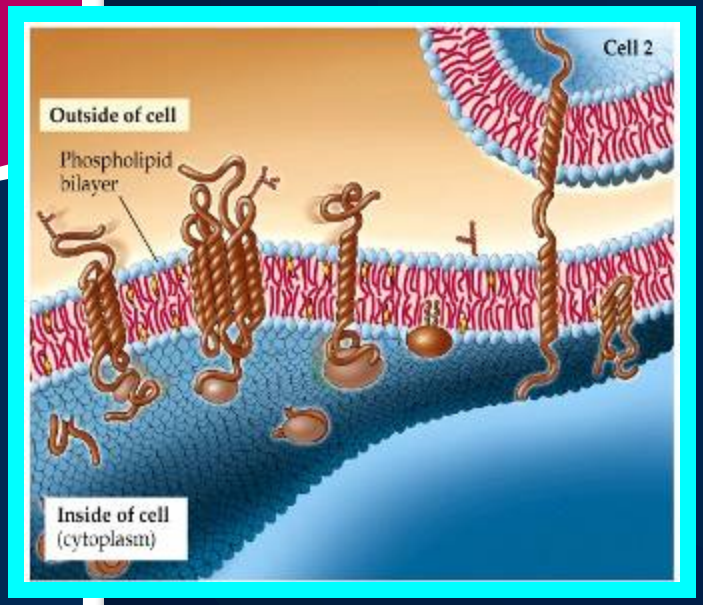
- *SCCM/ASPEN Guidelines:*
  - *Tolerance maybe enhanced with:*
  - *Δ from intact proteins $\Rightarrow$ small peptides*
  - *Δ from LCFAs $\Rightarrow$ MCTs or VLF diet*
- *Immunonutrition*
  - *Glutamine*
  - *Omega fatty-acids*

Ω-3 Fish Oils: Dietary Modulation of Inflammation





Neutrophil



- *Substitution of Ω-3 fish oil generates less inflammatory PGE_3, LTB_5, TxA_3 and reduces chemotaxis (neutrophil stimulation, activation, and recruitment key factor in AP)*
- *DHA inhibits intracell signaling, inflam cytokines, apoptosis, DNA fragmenting*
- *Many other mechanisms may contribute*

Ann NY Acad Sci 2009;1171:421

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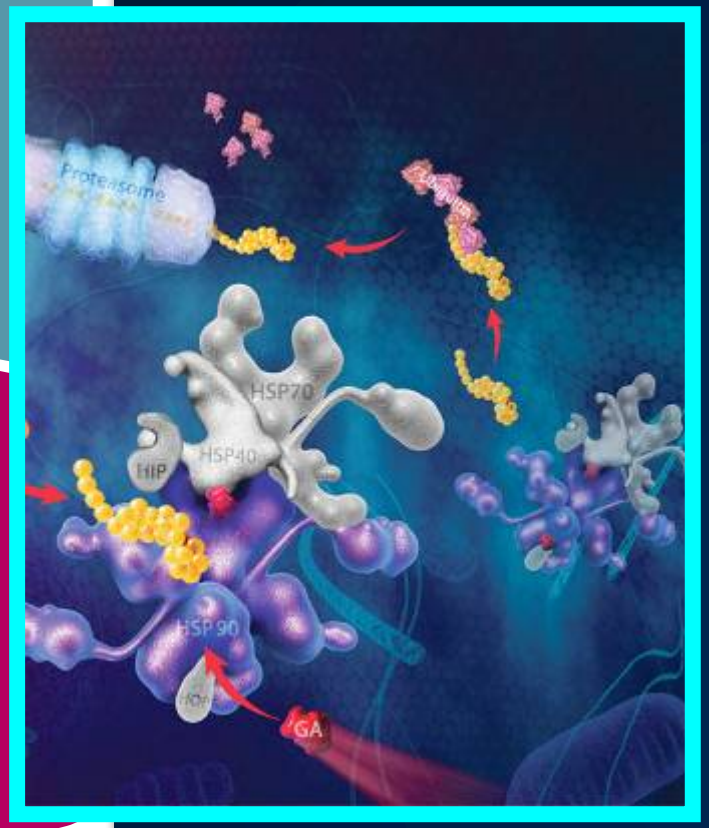
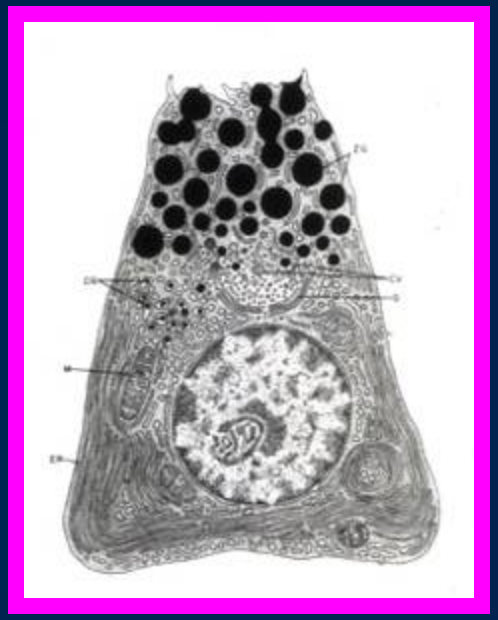
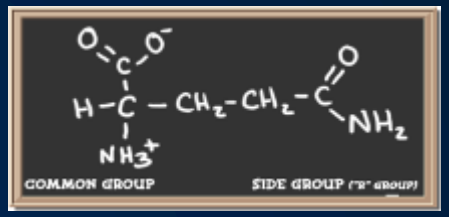
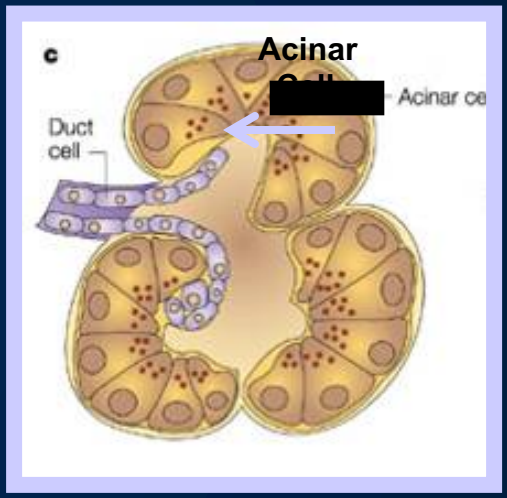
Role of HSPs in Pancreatitis







Glutamine



- HSPs upregulated in the acinar cell in AP
- Prior induction reduces severity of AP
- Mechanism: Prevents co-localization Blocks trypsinogen activation
  Prevents calcium rise Promotes apoptosis
  Blocks NF-kB (TLR-4)
- Diet modulation - Glutamine stimulates HSPs

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Pandol (Gastro 2007;132:1127) Bhagat (Gastro 2002;21:248)

In summary

- *Fluid resuscitation*
  - *Admission to an ICU/monitored setting for resuscitation*
  - *Crystalloid preferred over colloid*
  - *Aggressive and early fluid resuscitation is superior*
- *NG or NJ feeds*
  - *Equivocal, but early initiation*
- *Timing of initiation*
  - *Within 24 hours, when safe to do so*
  - *If patient can tolerate PO intake, regular diet should be initiated*
  - *TPN is limited to patients that cannot tolerate PO intake*

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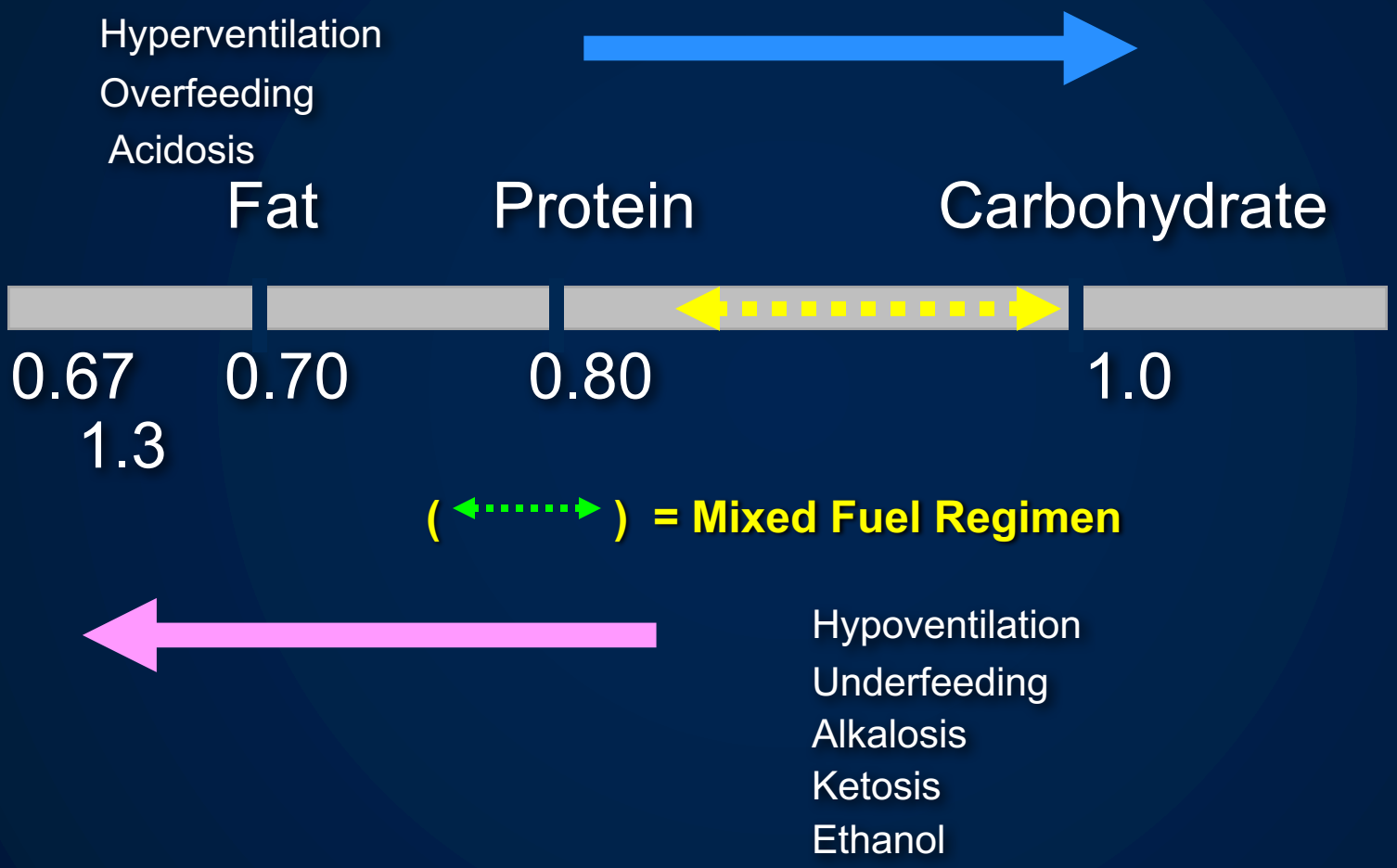
What Formula to Use?

- ***Elemental or peptide-type*** *formulas in the duodenum ⇓ pancreatic secretions by 50%*
- ***Clinical trials*** *⇒ peptide-based solutions*
- *Feeding higher in GI ⇒ more likely to stimulate pancreatic exocrine fx*
- ***40 cm or > below*** *the ligament of Treitz assoc. with little or* ***NO*** *stimulation*

Respiratory Quotient = VCO2 / VO2



Physiologic Range

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Thank-you!