DM SEMINAR
SEPTEMBER 23, 2005

NUTRITION IN ICU

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Scope of seminar

- Introduction
- Assessment of nutritional status
- Provision of nutritional support
- Enteral & Parenteral Nutrition
- Obesity & ICU
- Immunonutrition
- Nutrition Protocols

Introduction

- Critical illnesses, stress & surgery place ↑ demands on body's nutritional req.→ promote a catabolic state & -ve N balance.
- Prolonged bed rest & inactivity per se → -ve N balance in healthy individuals

  Bloomfield SA. Med Sci Sports Exerc. 1997; 29(2): 197-206.
- Combination of hypermetabolic state like critical illness or sepsis + bed rest & inactivity → suitable environment for occurrence of malnutrition

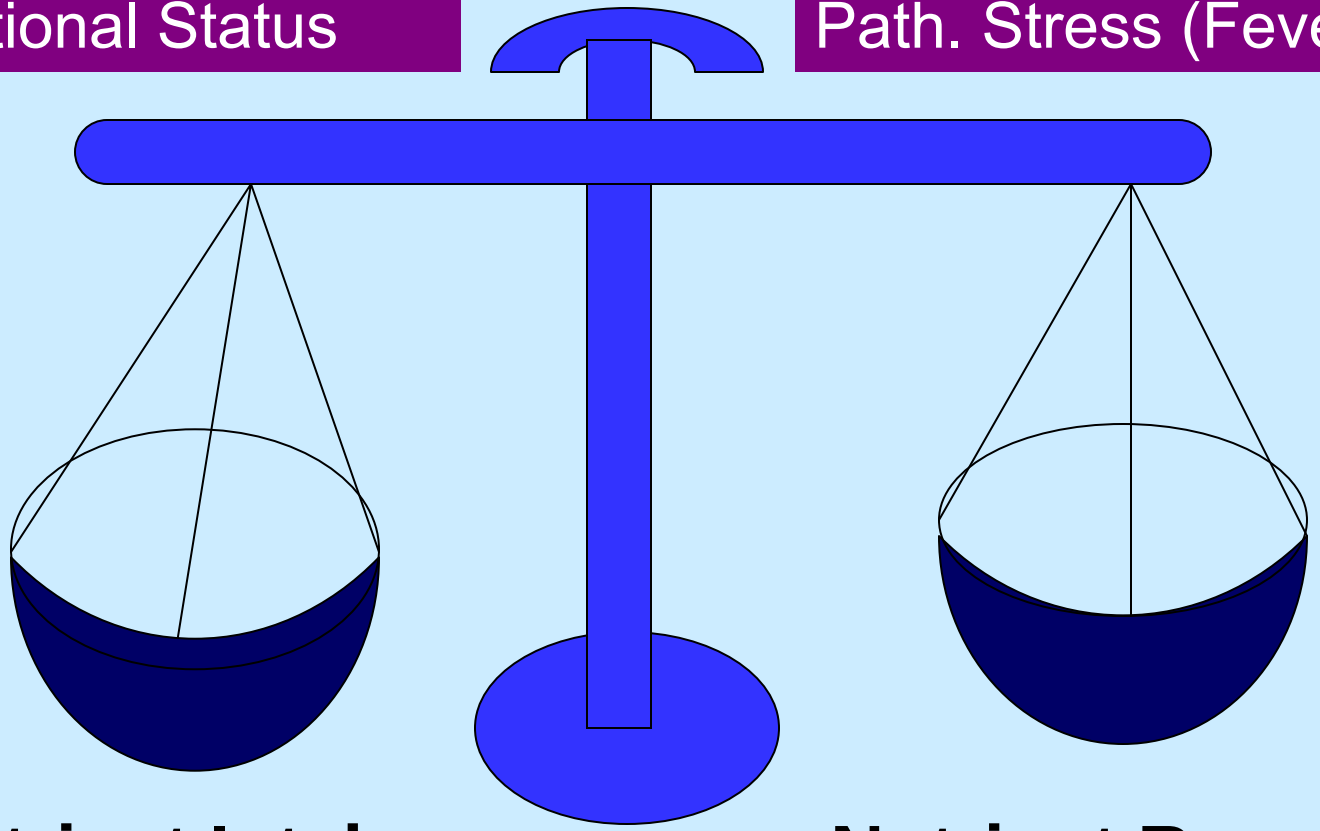
Introduction

- Malnutrition - net nutrient intake < net nutrient req
  - 1% to 15% of ambulatory outpatients
  - 25% to 60% of institutionalized patients
  - 35% to 65% of hospitalized patients
- Uncorrected it is succeeded by metabolic abnormalities, physiologic changes, reduced organ & tissue f_x & loss of body mass

OPTIMAL NUTRITIONAL STATUS & FACTORS INFLUENCING IT

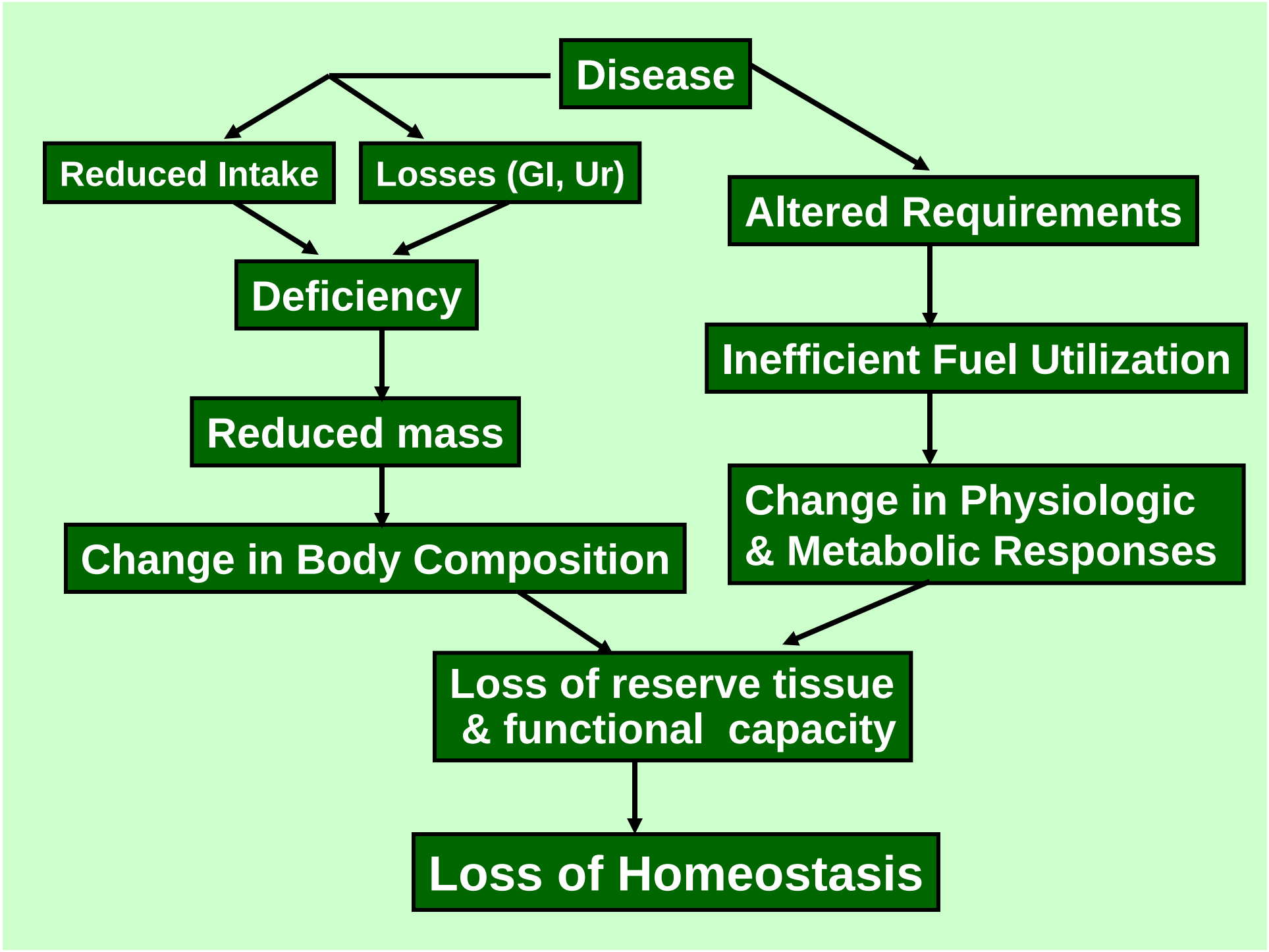
SE Status, Disease,
Cultural Factors,
Emotional Status

Physio. Stress (Preg, Growth)
Psychological Stress
Path. Stress (Fever, Disease)



Nutrient Intake

Nutrient Requirements


Disease
Reduced Intake
Losses (GI, Ur)
Altered Requirements
Deficiency
Inefficient Fuel Utilization
Reduced mass
Change in Physiologic & Metabolic Responses
Change in Body Composition
Loss of reserve tissue & functional capacity
Loss of Homeostasis

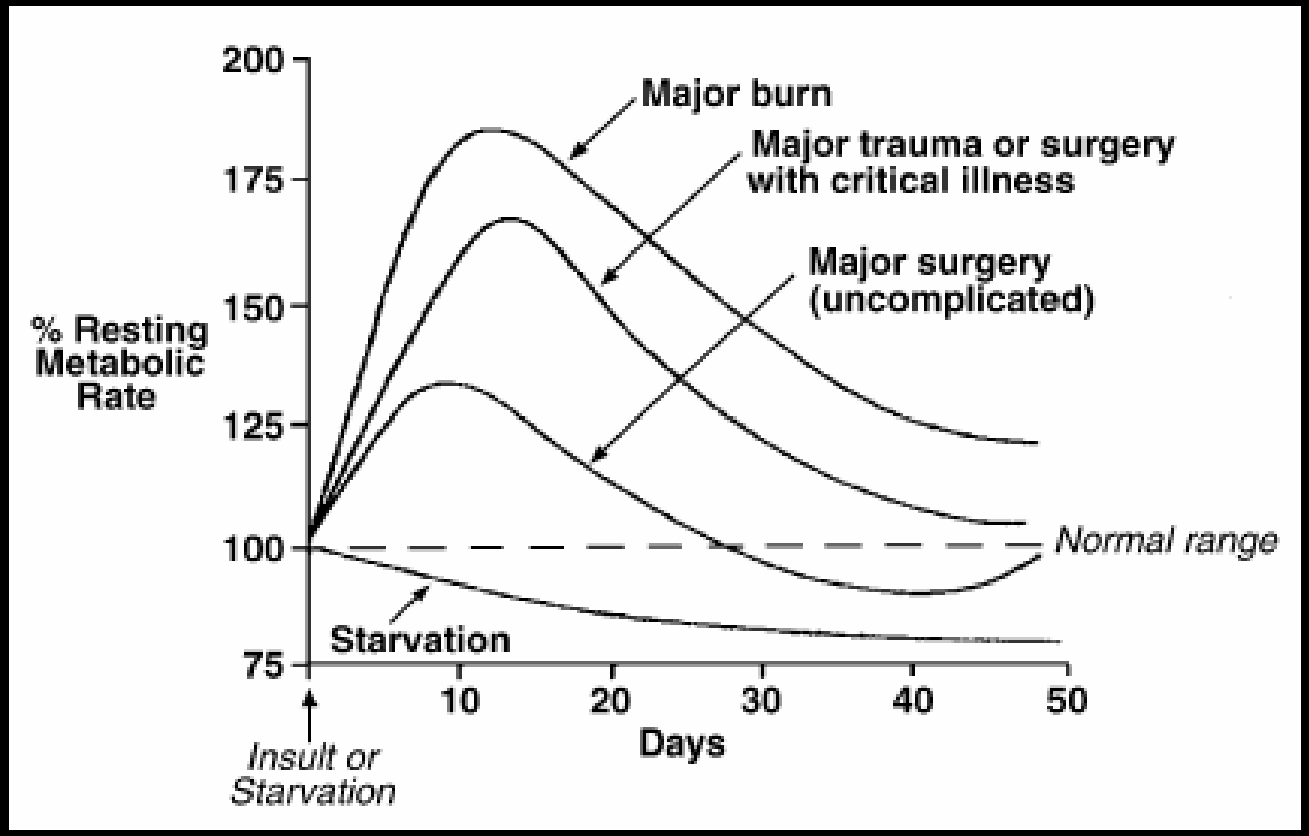
Introduction

- Effect on Liver:
  - Increased production of acute phase proteins
  - Decreased production of albumin
  - Increased catabolism of albumin
  - Extravasation of albumin into extravascular space
- Effect on Lungs :
  - Decreased diaphragmatic muscle mass
  - Decreased max voluntary ventilation
  - Decreased max mouth pressures
  - Breathing pattern (Rapid shallow)
  - Increased Fluid in Interstitium
  - Decreased FRC & predisposition to atelectasis

Introduction

Feature	Starvation	Catabolism in Critical Illness
BMR/REE	↓	↑
Resp. Quotient	(0.6-0.7)	(0.8-0.9)
Cytokine levels	↓	↑
Primary fuels	Fat	Mixed
Proteolysis	+	+++
Ureagenesis	+	+++
Ur N losses	+	+++
Gluconeogenesis	+	+++
Ketone production	+++	+

Introduction



Demling RH, DeSanti L. Curr Opin Crit Care 1996; 2: 482–491

Introduction

- Factors adversely influencing outcome in critical illness
  - Depleted lean body mass
  - Male gender
  - Insulin insensitivity
  - Impaired anti-oxidant defences
  - Immunosuppression
  - Hyper inflammatory state
  - Ageing
  - 'Disadvantageous genotype'

Grimble RF. Curr Opin Gastroenterol 2005; 21: 216–222

Introduction

- Malnutrition in ICU patients can be either present on admission or develop subsequently as a result of metabolic response to injury
- Whatever the cause the end result is the same i.e. malnourished pts tend to have longer hospital LOS → ↑ costs of care & mortality

Middleton MH et al. Intern Med J. 2001; 31(8): 455-461.

- Nutritional suppl → opportunity to slow down or halt catabolism → restore N balance → prevent malnutrition

Nutritional Assessment

Nutritional Assessment

- History:
  - Medical (ch debilitating diseases & psy disorders)
  - Socioeconomic
  - Dietary/nutritional
  - Drug abuse & alcoholism
- Physical Examination:
  - Nutrition focused physical examination
  - Anthropometry
  - Body composition & circumference measurements
- Laboratory Investigations:
  - Biochemical
  - Immunologic

Nutritional Assessment

Body Weight:

- Unintentional loss of usual BW by >10% in 6 m (or >5% in 1 m) clinically significant & suggestive of malnutrition
- Problems with BW:
  - Critically ill pts often edematous (water & salt retention) → BW changes usually reflect fluid shifts & not changes in actual body cell mass
  - Based on comparison with a wide range of N values compounded by presence of diversity in control population

Nutritional Assessment

1. Ideal BW: comparison of ABW with IBW more useful than ABW alone

   IBW (M) = 106 lb for 5 ft height + 6 lb/ each addl inch

   IBW (M) = 47.3 kg for 150 cm height + 2.7 kg/ each addl 2.5 cm

   IBW (F) = 100 lb for 5 ft height + 5 lb/each addl inch

   IBW (F) = 44.6 kg for 150 cm height + 2.2 kg/each addl 2.5 cm

   Add or subtract 10% for large & small frames resp

2. **BMI:** Useful for grading malnutrition & prognostication

Nutritional Assessment

BMI (in kg/m^2)	**Nutritional Status**
>30	Obese
25-30	Overweight
20-25	Normal
<18.5	Mild & moderate malnutrition
<16	Severe malnutrition
<13	Usually incompatible with life (M)
<11	Usually incompatible with life (F)

Henry CG. BMI & limits of human survival. Eur J Clin Nutr 1990; 44: 329-335

Nutritional Assessment

- Anthropometric measurements:
  - Objective evaluation of fat & LBM/skeletal proteins
  - Safe, simple & inexpensive
  - Can be done at bedside
  - ? Reliability – Accuracy of detecting ac changes esp critically pts who receive aggressive fluid resuscitation

1. Skinfold thickness
   - Based on assumption that 50% of total body fat is s/c (vary from 20-70% in N subjects)

Nutritional Assessment

- Commonly triceps used (subscapular/ iliac crest/ upper thigh) → N values = 12.5 mm (M) & 16.5 (F)
- Over & under-estimation of body fat in malnourished & obese pts respectively

2. Mid upper arm circumference (MUAC):
   - Mid-point b/w acromion & olecranon
3. Mid arm muscle circumference:

   = MUAC – { π x TSF }
   - N values = 25.5 mm (M) & 23.0 mm (F)
4. W/H ratio

Nutritional Assessment

Serum Albumin

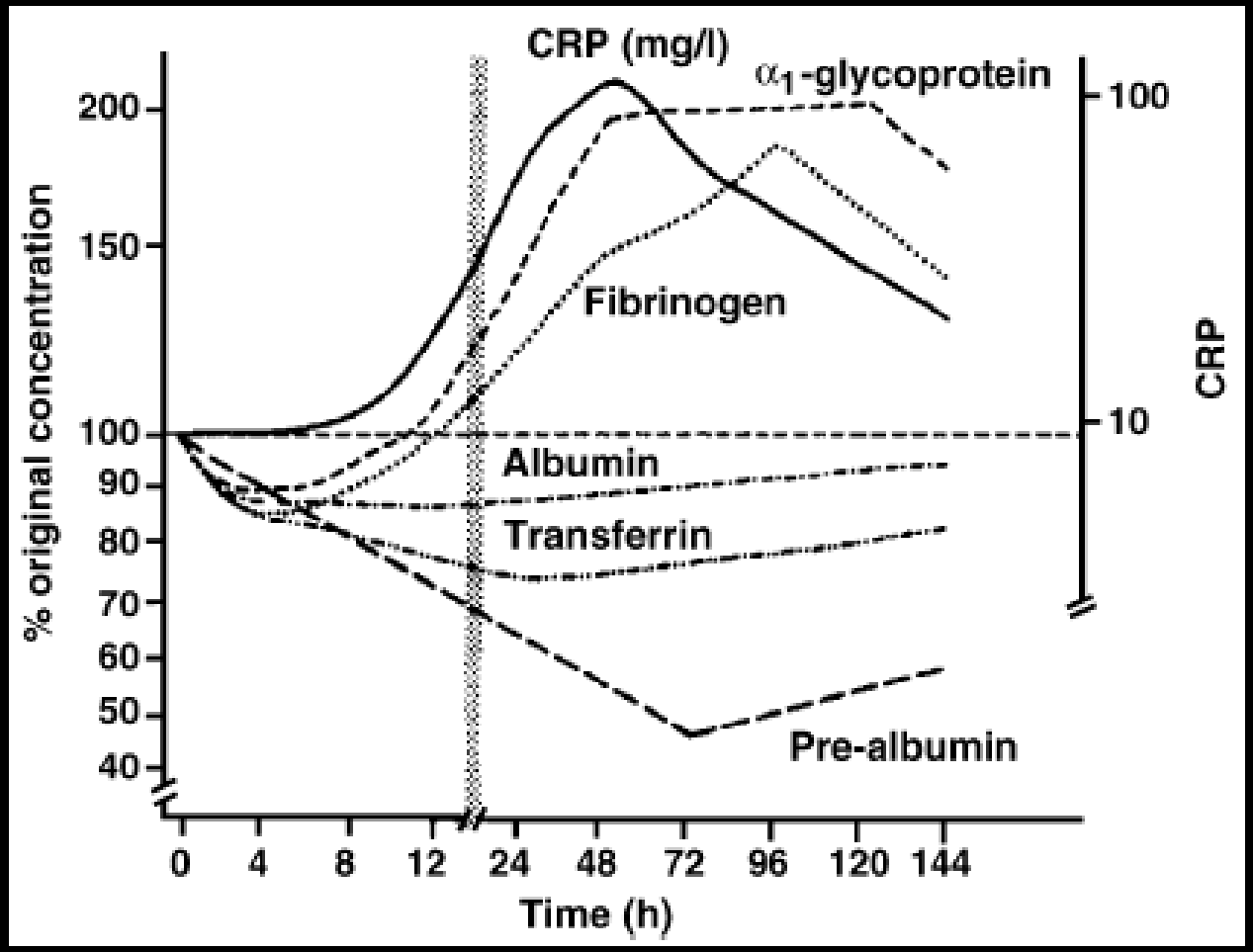
- Serum half life 20 d
- Neither sensitive nor specific as a std for nutritional assessment
- In addition to nutritional status, affected by:
  - Hepatic f_x
  - Protein loss
  - Hydration status
  - Changes in distribution b/w intra & extravascular compartments incl exudation at the capillary level
  - Infection/infl
- Better marker of disease severity than nutritional status?

Nutritional Assessment

Serum Albumin

- Hypoalbuminemia an imperfect measure of nutrition but an excellent marker of injury?
  - ↓ Levels indicate ↑ catabolism (cytokine mediated)
  - Levels correlate inversely with other markers of infl
  - Rate of fall may be as high as 50% in 2 d of ac phase of sepsis & can relate to mortality
  - Levels not expected to ↑ despite ↑ nutritional intake unless stress response subsides → Attempts at correction of hypoalbuminemia by i/v admn of albumin not assoc with improved clinical outcomes

Serum proteins in critical illness



Fleck A. Br J Clin Pract Suppl 1988;63:20–4;

Nutritional Assessment

Serum Albumin

- Control of stress → levels can ↑ by upto 10%/ day with adequate nutr support → may be N by 2 wks

- However despite the concerns regarding its usefulness, "serum albumin remains one of the most powerful nutritional markers & outcome predictors in hospitalized patients & critical illness"

Lafrance JP et al. Metabolic, Electrolytes & Nutritional Concerns in Critical Illness. Crit Care Clin 2005; 21: 305–327

Nutritional Assessment

- ALC:
  - Levels <1000/uL→ ? depletion of T cell rich areas of RES & assoc with cutaneous anergy
- Pre albumin:
  - Produced primarily in liver (others – choroid plexus & enterochromaffin cells in GI mucosa)
  - Normal levels: 6 to 35 mg/dl
  - ? Better marker of malnutrition
    - Short serum $t_{½}$ (2 days)
    - Less affect by liver disease than other proteins
    - Not affected by hydration status
    - Not affected by vitamin deficiency (except zinc)
    - Negative acute phase reactant

Nutritional Assessment

- SGA (Subjective Global Assessment):
  - Based on assumption that history/physical exam assesses nutritional status more precisely & is better predictor of morbidity/mortality than any lab test

- History:
  - Wt change
  - Dietary intake change (~ N)
  - GI symp (> 2 wks)
  - Functional capacity

- Physical Exam:
  - Loss of s/c fat
  - Muscle wasting
  - Ankle & sacral edema
  - Ascites

Nutritional Assessment

- Divided into
  - Class A :< 5% wt loss or > 5% wt loss + recent gain & improvement in appetite
  - Class B : 5-10% wt loss without recent stabilization or gain, poor dietary intake & mild loss of s/c tissue
  - Class C: ongoing wt loss of >10% with severe s/c tissue loss & muscle wasting often with edema

- Other Nutritional Indices:
  - Prognostic Nutritional Index (PNI) combines measurements of S. Albumin, S. Transferrin, TSF Thickness & Delayed Cutaneous Hypersensitivity
  - Prognostic Infl & nutritional index (PINI) aggregates S. levels of CRP, alpha 1-acid glycoprotein, prealbumin & albumin

Nutritional Assessment

- No single marker till date has been validated as being ideal for assessing nutritional status of critically ill patients i.e. there is no 'gold std':
  - No universally accepted clinical definition of malnutrition
  - All currently available parameters for assessment of nutritional status are affected by disease processes
  - Effects of malnutrition & of the disease itself on the final outcome may be difficult to distinguish
  - There is paucity of data to compare different commonly used nutritional assessment parameters and hence sensitivity, specificity and reliability of each vis-à-vis others cannot be defined

Klein S et al. J Parenter Enteral Nutr 1997; 21: 133-156

Provision of Nutritional Support

Provision of Nutritional Support

Goals/Principles of Nutr. Support to critically ill:

- Provision of nutr support after taking into account:
  - Medical condition
  - Baseline nutritional status
  - Existing metabolic requirements
  - Route available for admn of nutrients (EN and/or PN)
- Prevention (if possible) of nutrient deficiencies (macro & micro) & Rx of existing ones
- Avoidance of complications associated with nutritional support
- Improvement in pt outcomes (morbidity/mortality)

Provision of Nutritional Support

- Indications
  - Presence of malnutrition (of any etiology) in a patient unable to eat (Benefit of nutritional support best seen in pts whose baseline nutritional status is < N incl pts with BMI<16)
  - In well-nourished pts, prolonged fasting (>3-4 d) & inability to resume oral nutrition (Such pts can often tolerate short periods of starvation – <1 week)
  - Supplementation if oral intake insufficient for >3-4 d

Provision of Nutritional Support

- Sys review, 15 prospective RCTs, n=753
- Adult ICU pts (post-op, trauma, head-injury & burns) - No study on MICU pts
- Compared early EN (initiation of nutr support in < 36 hrs) to delayed EN (>36hrs)
- Early EN assoc with:
  - ↓ infection rates (RR = 0.45)
  - ↓ Hosp LOS
  - ↓ mortality (8% vs 11.3%, RR=0.74 NS)
- No diff w.r.t non-infectious complications

Marik PE et al. Crit Care Med 2001; 29(12): 2264-2270

Provision of Nutritional Support

Calories:

- TEE = REE x activity factor
- REE (BMR):
  - Harris-Benedict equation
    - Males = 66.5 + 13.75W + 5.003H – 6.775A
    - Females = 655.1 + 9.563W + 1.850H – 4.676A

      W = Wt in kg, H = Ht in cm & A = age in yrs
  - Males = 25 kcal/kg OR 900 + 10 x weight (kg)
  - Females = 22 kcal/kg OR 700 + 7 x weight (kg)
  - Fever → ↑ 10%/°C rise in temp
  - Sepsis → ↑ by 40 – 100%
  - Starvation → ↓ by 20 – 40%

Provision of Nutritional Support

- Activity factor:
  - 1.2 (sedentary), 1.4 (moderate) & 1.8 (heavy)
- Indirect calorimetry:
  - Measures REE from O_2 consumption (VO_2) & CO_2 production (VCO_2) in specified time period

$$REE\ (kcal/min) = C.O. \times VO_2 + 1.1\ VCO_2$$

$$REE\ (kcal/d) = REE\ (kcal/min) \times 1440$$

Protein:

- 1.2-1.5 g/kg BW/d (max 1.8-2.0 g/kg BW/d in pts with extreme protein losses

Fluid: Approx 1 ml of water per kcal administered

Enteral & Parenteral Nutrition

Enteral & Parenteral Nutrition

- Whenever nutritional supplementation is indicated, EN preferred to PN
- Advantages of EN over PN:
  - ↓ incidence of mucosal atrophy & reduction in ↑ intestinal permeability
  - Promotes gut motility → paves way for initiation of oral feeding
  - ↓ translocation of bacteria from the gut
  - Avoids infectious complications assoc with PN
  - Less costly
  - More physiological

Jolliet P et al. Intensive Care Med 1998; 24: 848-859

Enteral & Parenteral Nutrition

- Contraindications to EN:
  - Absolute
    - Nonfunctional gut: anatomic disruption, obstruction, gut ischemia
    - Generalized peritonitis
    - Severe shock states
  - Relative
    - Expected short period of fast, except in severely injured patients
    - Abdominal distension during EN
    - Localized peritonitis, intra-abdominal abscess, severe pancreatitis

Early EN vs Early PN

- Meta-analysis of trials comparing early EN vs early PN in hospitalized pts
- 30 RCTs (10 medical, 11 surgical & 9 trauma)
- No diff b/w groups in terms of hospital mortality (applicable for subgroups also)
- PN → ↑ incidence of infective (incl CRBI) & noninfective complications & Hosp LOS
- EN assoc with ↑ in diarrhea
- No effect of age, time to initiate Rx & av albumin on mortality
- "Early EN ~ early PN does not ↓ mortality"

Peter JV et al. Crit Care Med 2005; 33(1): 213-220

Enteral vs Parenteral Nutrition

- Meta-analysis of 11 trials (complete F/U in 9) of PN vs. EN in critically ill pts
- Analysis based on intention to treat principle
- Mortality benefit in favour of use of PN; subgroup analysis → benefit from PN use greatest in trials in which EN delayed (>24 hr)
- Infectious complications increased with PN (6/9)
- "Grade B+ EB recommendation for PN use in pts in whom EN cannot be initiated within 24 hr of ICU admission or injury"

Simpson F et al. Intensive Care Med 2005; 31: 12–23

Enteral vs Parenteral Nutrition

- Sys Review,13 RCTs, n=807
- Compared EN vs PN for outcome of critically ill adult pts
- Heterogeneous population of ICU pts (head trauma & injury, abd trauma, sepsis, cardiac bypass or severe ac pancreatitis)
- Use of EN ~ PN assoc with
  - ↓ in infectious complications (RR = 0.64)
  - ↓ in cost
- No diff in mortality, MV duration or hosp LOS

Gramlich L et al. Nutrition 2004;20:843– 848

Enteral vs Parenteral Nutrition

- PN assoc with:
  - ↑ incidence of hyperglycemia
  - ↑ caloric intake (5/11)
- No diff in mortality rate b/w pts on PN & ↑ BS vs pts on EN & N BS
- Data on baseline nutritional status NA → no conclusion on its relation with outcome
- "EN should be the first choice for nutritional support in the critically ill"

Gramlich L et al. Nutrition 2004;20:843– 848

Enteral + Parenteral Nutrition

- Sys review, 5 RCTs, n=248, ICU (M + S), Burns & Blunt Trauma pts
- Compared EN + PN to EN alone (PN started at same time as EN)
  - No diff b/w groups w.r.t mortality, rates of infection, Hosp LOS or MV duration
  - EN + PN → significant ↑ in cost & calorie delivery
- "In critically ill patients who are not malnourished and have an intact gastrointestinal tract, starting PN at the same time as EN provides no benefit in clinical outcomes over EN alone"

Dhaliwal R et al. Intensive Care Med 2004; 30: 1666–1671

Enteral & Parenteral Nutrition

- “PN remains a valuable yet challenging weapon in our therapeutic armory in the presence of GI feed intolerance or failure. However it should be used wisely & not indiscriminately because most intensive care patients with a fully functional GIT may be fed safely with EN”

Griffiths RD. Curr Opin Clin Nutr Metab Care 2004; 7:175-181

Obesity in ICU

- Predicting energy needs in critical illness difficult (uncertainties reg influence of diff factors on EE) → much more difficult in critically ill obese pts
- Although morbidly obese patients have excess body fat stores, they are prone to develop protein malnutrition during metabolic stress
- ↑ basal insulin level → suppression of lipid mobilization from body stores → acc protein breakdown for gluconeogenesis → rapid ↓ in lean body mass (LBM) & ↑ in urea prod & Ur N losses

Jeevanandam M et al. J Clin Invest 1991; 87: 262–269

Obesity in ICU

Effect of obesity on ICU mortality

- Retro study (n=117, 2 MICUs)
  - Morbidly obese pts (BMI>40) had ↑ req for MV, MV duration, ICU LOS & overall mortality (30% vs 17%)

    El-Sohl A et al, Chest 2001; 120:1989–1997
- Prospective study (n = 813, single center)
  - BMI of 27 used to separate obese (n = 215) & nonobese (n = 598) groups
  - Obese pts had higher ICU LOS, SAPS II score & ICU mortality. Observed mortality of obese pts > mortality predicted by SAPS II scores

Obesity in ICU

- Multivariate analysis → SAPS II score & BMI > 27 predictive of ICU mortality
- "Current prognostic scoring systems do not include BMI/obesity though high BMI value is an independent predictor of high ICU mortality → These underestimate the mortality risk for obese patients"

Goulenok C et al. Chest 2004; 125: 1441–1445

- Prospective study (n= 2148)
  - No effect of BMI on APACHE II scores, mortality, ICU LOS, hospital LOS, % req MV, days on MV, total cost or adverse events
  - "BMI has minimal effects on ICU outcome"

Ray DE et al. Chest 2005; 127: 2125–2131

Obesity in ICU

- SUPPORT (Study to Understand Prognoses & Preferences for Outcomes & Risks of Rx)
  - Prospective, multicenter study (n = 4301)
  - 5 tertiary care medical centers
  - Pts >18 yrs + anticipated 6 m mortality = 50%
  - BMI <15th percentile assoc with ↑ 6 m mortality (risk ratio = 1.23)
  - High BMI (>85th percentile) not assoc with significantly ↑ risk of mortality

Galanos AN et al. Crit Care Med 1997; 25:1962-1968

Obesity in ICU

- Retrospective analysis (n = 41011, Multicenter)
  - Divided into 2 groups depending whether SAPS II or mortality prediction model [MPM] used
  - Underweight (BMI <20) → ↑ mortality + ↑ ICU & hospital LOS + Impaired f_x status at discharge
  - Overweight (BMI = 25-30) → ↓ disability at discharge
  - Obese (BMI = 30-40) → ↑ ICU & hospital LOS (SAPS) BUT ↓ disability at discharge (MRM)
  - Severely obese (BMI > 40) → ↑ ICU & hospital LOS
  - "Overweight & Obese Pts may have ↓ mortality & improved functional status at discharge"

Tremblay A et al. Chest 2003; 123: 1202–1207

Obesity in ICU

- Which weight to use?
- ABW vs IBW
  - 65 hospitalized & 65 non hospitalized obese adults (ABW >130% IBW, ~ all pts on EN/PN)
  - EE predicted better by using ABW ~ IBW

Ireton Jones et al. J Am Diet Assoc 1991; 91: 93-95

- Obesity Adjusted Wt (OAW)
  - Developed for more accurate prediction of LBM in obese pts

OAW = IBW + 0.25 (ABW – IBW)

Obesity in ICU

- OAW vs ABW
  - Energy needs predicted with Harris-Benedict equation (HBE) & kJ/kg (KPK) strategies (using both ABW & OAW)
  - Results compared with measured EE determined by indirect calorimetry
  - Use of ABW → overfeeding
  - Use of OAW + KPK strategy → more accurate energy predictions ~ HBE
  - OAW + KPK strategy preferable for obese pts (≥ 130% of IBW)

Cutts ME et al. Am J Clin Nutr 1997; 66: 1250–1256.

Obesity in ICU

- Eucaloric vs hypocaloric EN
  - 40 critically ill, obese pts admitted to trauma/SICU (ABW > 125% of IBW)
  - Eucaloric feeding (≤ 20 kcal/kg/d of OAW) or hypocaloric feeding (>20 kcal/kg/d of OAW)
  - Protein intake for both ~ 2 g/kg/d (IBW)
  - Hypocaloric group:
    - Shorter ICU LOS
    - ↓ Duration of Antibiotic Rx
    - ↓ Duration of MV (NS)

Dickerson RN. Nutrition 2002; 18(3): 241-246.

Obesity in ICU

- Indirect calorimetry to determine EE :
  - Req FiO_2 <0.6
  - Erroneous values:
    - System leaks
    - Abnormal water vapor pressure
    - Errors in calibration
- Current recommendation:
  - OAW + KPK strategy
  - 20 – 30 kcal/kg/d (OAW)
  - 1.5–2.0 g/kg/d (IBW)

El-Solh AA. Am J Respir Crit Care Med 2004; 169: 557–561

Immunonutrition

Immunonutrition

- Nutritional deficits produce significant atrophy of lymphoid organs & impaired fx
- MaInutrition (& impaired immune f_x) common in hospitalized patients → adverse effect on recovery
- The administration of nutrients that have nutritive and pharmacological effects (immunonutrition) can counteract this and improve patient outcome
- Immunonutrients are specific nutrients that exert immune enhancing effects independent of their energy/protein value (include arginine, glutamine, nucleotides & ω-3 FA)

Immunonutrition

Immunonutrient	Mode of action
n-3 (omega-3) fatty acids (principally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).	Anti-inflammatory by suppressing pro-inflammatory cytokine production; reverses immunosuppression.
Sulphur amino acids, their precursors and other thiol compounds (Methionine, cysteine, *N*-acetyl cysteine (NAC), L-2-oxothiazolidine-4-carboxylate lipoic acid (OTZ; procysteine).	Enhances antioxidant defences via glutathione synthesis or 'protection' of available glutathione (GSH) through provision of other sulphydryl groups to interact with oxidant molecules.
Glutamine	Nutrient for immune cells, improves gut barrier function, non-sulphydryl precursor for GSH.
Arginine	Precursor for nitric oxide, enhances T lymphocyte numbers and function, precursor for praline, stimulates growth hormone production.
Nucleotides	RNA and DNA precursors, improves T lymphocyte function.

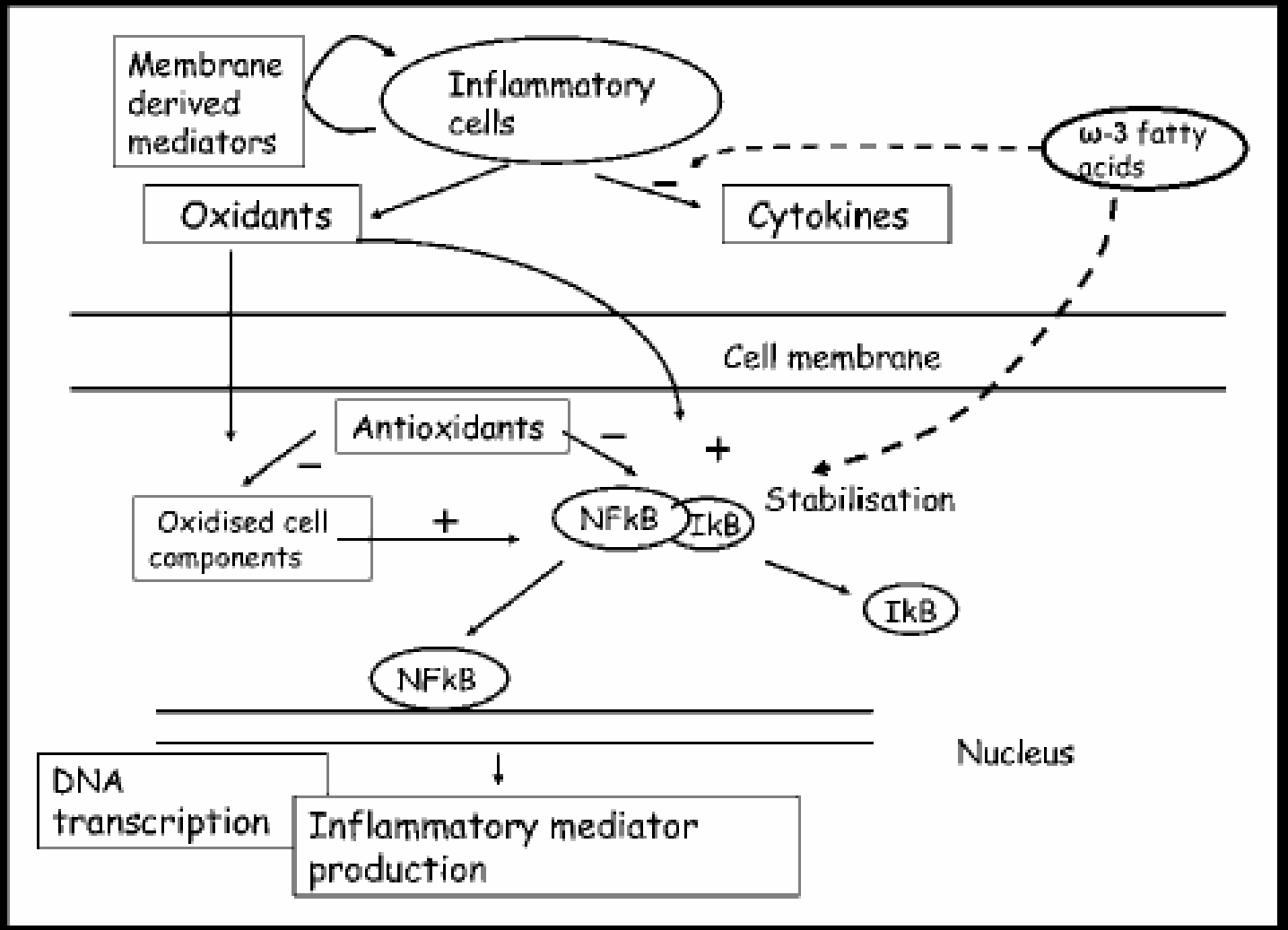
ω-3 FA + med chain TGs + olive oil
alt to ω-6 FA (pro-infl effects)
as I/V lipid suppl

Oxidative fuel for lympho & macro.
During stress, exogenous glutamine reqd to avoid catabolism & muscle glutamine depletion

Stimulation of macrophages
& NK cells fx

Grimble RF. Immunonutrition. Curr Opin Gastroenterol 2005; 21: 216–222

Antioxidants/ω-3 FA & Oxidative/Inflammatory Stress



Grimble RF. Immunonutrition. Curr Opin Gastroenterol 2005; 21: 216–222

Immunonutrition

- Linoleic acid
  - ω–6 PUFA
  - Major constituent of cell membranes
  - Precursor of prostanoid & LT synthesis
  - No parenteral forms available
- Trace Elements
  - Zinc reqd for biologic activity of thymic hormone (T cell maturation) → Def assoc with intractable infections
  - Copper → Effects on T & B cell function
  - Selenium def → ↓ Ab responses
  - Other trace elements & antioxidants shown *in vitro* to modulate activity of various immune cells

Slone DS. Crit Care Clin 2004; 20: 135–157

Immunonutrition

What is clear about Immunonutrition?:

–Efficacy better when admn through EN > PN

–Efficacy better when admn to malnourished pts

What is unclear?

Is it efficacious at all?

Immunonutrition

- Meta-analysis, 11 RCTs, n=1009
- Comparison of EN + key nutrients vs std EN in pts with critical illness & cancer
- Results:
  - ↓ in infectious complications
  - ↓ hosp LOS
  - No diff in mortality
  - No diff in incidence of pneumonia

Heys SD et al. Ann Surg. 1999; 229(4): 467-77

Immunonutrition

Outcome	No of trials		Effect of ImN	
	Overall	Medical	Overall	Medical
Mortality	12	3	NS	NS
Infection	8	1	↓S	NS
Hosp LOS	10	2	↓ HS	↓ S
ICU LOS	6	2	NS	NS
Days on MV	5	2	↓ S	NS

Comparison of outcome with std EN vs commercially available immune-enhancing EN feeds (arginine ± glutamine, nucleotides & ω-3 FA) in critically ill pts after trauma, sepsis or major surgery
Sys review (12 RCTs, n=1482), analysis on intent-to-treat basis

Beale RJ et al. Crit Care Med 1999; 27:2799-2805

Immunonutrition

Outcome	No of trials		Effect of ImN	
	Overall	Medical	Overall	Medical
Mortality	22	13	NS	NS
Infection	18	9	↓ **S**	NS
Hosp LOS	17	8	↓ **S**	↓ **S**

Comparison of outcome of std EN vs EN + immune enhancing nutrients in pts of elective surgery & critically ill pts after trauma, burns or in ICU, Sys review (22 RCTs, n=2419)

Use of formulas other than high arginine content → ↑ mortality & ↑ hosp LOS (overall & critically ill pts)

Use of high arginine content formulas → ↓ infection (overall) & ↓ hosp LOS (overall & critically ill pts)

Heyland DK et al. JAMA 2001; 286: 944-953

Immunonutrition

- Sys review of effects of std EN vs diets enriched with pharmaconutrients
- 26 RCTs – surgical (9), trauma (7), burns (2) & mixed/ICU (8) – n=?
- Overall: Pts in pharmaconutrition group had ↓
  - Incidence of HAP (11, OR=0.54)
  - Incidence of bacteremia (9, OR=0.45)
  - MV duration (7), ICU LOS (8) & Hospital LOS (12)
- No diff in mortality (18) – overall & subgroup analysis
- No diff in incidence of sepsis (5) or UTI (10)

Montejo JC et al. Clin Nutr. 2003; 22(3): 221-233

Immunonutrition

- No e/o ↓ total no of infected pts during ICU stay (ONLY ↓ incidence of some infections in some groups)
- Mixed group – No ↓ MV duration, Hosp LOS or ICU LOS in pharmaconutrient group
- Marked heterogeneity in patient characteristics as well as methodology/designs of trials
- "Considering some beneficial effects & absence of detrimental ones, these diets could be recommended in ICU pts requiring EN (Grade B recommendation)"

Montejo JC et al. Clin Nutr. 2003; 22(3): 221-233

Immunonutrition

- Prospective DB RCT
- 2 ICUs, Netherlands
- Heterogeneous population of pts expected to require EN > 48 hrs (n =597)
- Randomized to receive Immunonutrition (high-protein enteral formula enriched with arginine, glutamine, ω3-FA & antioxidants) or an isocaloric control formula
- Intention to Rx analysis

Kieft H et al. Intensive Care Med. 2005; 31(4): 524-532

Immunonutrition

- No diff b/w groups w.r.t.:
  - Hosp LOS
  - ICU LOS
  - MV duration
  - ICU mortality
  - Hosp mortality
  - Infectious complications
- "Largest RCT on immunonutrition → in a general ICU population immunonutrition has no beneficial effect on clinical outcome parameters"

Kieft H et al. Intensive Care Med. 2005; 31(4): 524-532

Immunonutrition

Q: Why is there so much variability in responsiveness to immunonutrition?

A: Genes for cytokines & other molecules that influence infl may be affected by changes in their promoter regions [single nucleotide polymorphisms (SNP)] → diff in amount of gene formed when activation occurs. In addition to diff in pt profiles, SNPs may be an imp factor determining efficacy & clinical outcomes of immunonutrition → studies reqd to determine exact nature of genomic factors that influence immunonutrition

Immunonutrition

- Reports of ↑ infl could counteract effect on ↑ immunity & could even make overall responses to immune enhancing diets harmful
- Effects are potentially unpredictable in different clinical settings → Avoid extrapolation of results between disparate groups
- Routine use of immune-enhanced formulas cannot be recommended without further research to define the underlying mechanisms by which immunonutrition may be harmful & to identify which ingredients have beneficial effects

Nutrition Protocols

Nutrition Protocols

- Pros:
  - Era of EBM → Use of guidelines, clinical protocols & recommendations → improved quality of care (esp in critical care – single intervention → dramatic consequences & amount of available info > human decision-making limits)
- Cons:
  - Shortage of large prospective RCT → limitation in stringency of recommendations
  - ? Compliance with 'tight stds of care' → Imposition of "cookbook medicine" → hampered freedom of Mx of pts
  - "Anorexia Protocolis" (reluctance to use protocols)

Zaloga et al. Chest 2004 ; 125 : 1195–1196

Nutrition Protocols

- Prospective observational study
- Canada, 59 ICUs (n = 638)
- Hypothesis: ICUs whose practice was more consistent with guidelines would have greater success in providing EN
- Pts on MV > 48 hrs & ICU stay > 72 hrs
- Av duration of observation ≈ 10 d
- Adequacy of EN (received/prescribed calories) = 1.8-76.6% (av 43%)

Heyland DK et al. Crit Care Med 2004; 32(11): 2260-2266

Nutrition Protocols

- Higher adequacy of EN assoc with:
  - Use of a feeding protocol
  - Early initiation of EN (>50% of pts within 1st 48 hrs)
  - Use of small bowel feedings or motility agents in >50% of pts with high gastric residual vol
  - Inverse assoc with ↑ use of PN (> median)
- Study confirmed hypothesis: ICUs that are more consistent with clinical practice guidelines are more likely to successfully provide EN support to pts → could lead to better outcomes

Heyland DK et al. Crit Care Med 2004; 32(11): 2260-2266

Nutrition Protocols

- Prospective study
- USA, MICU/SICU of 2 teaching hospitals
- Objective: To determine effect of implementation of an EB nutritional Mx protocol in ICU
- Included all pts with expected ICU stay > 48 h
- n= 200, 100 pts in each group (before & after implementation of protocol)
- Pts in postimplementation group:
  - Fed more frequently via enteral route (adjusted OR = 2.4)
  - Shorter duration of MV

Barr J et al. Chest 2004; 125: 1446–1457

Nutrition Protocols

- No diff between two groups:
  - Time to initiate feeding
  - Total caloric intake on d 4 of nutritional support
  - ICU LOS
  - Hospital LOS
- Pts who received EN had ↓ risk of death (HR = 0.44)

Barr J et al. Chest 2004; 125: 1446–1457

Nutrition Protocols

- ACCEPT (Algorithms for critical care enteral & parenteral therapy) Trial
  - Multicentre, cluster RCT (n = 462)
  - Hypothesis: Use of EB algorithms for providing nutritional support in ICU → improvement in pt outcomes
  - ICUs of 12 hospitals
  - Pts ≥ 16 yrs & expected ICU LOS > 48 hrs
  - ICUs stratified by hospital type & randomized to intervention or control arms

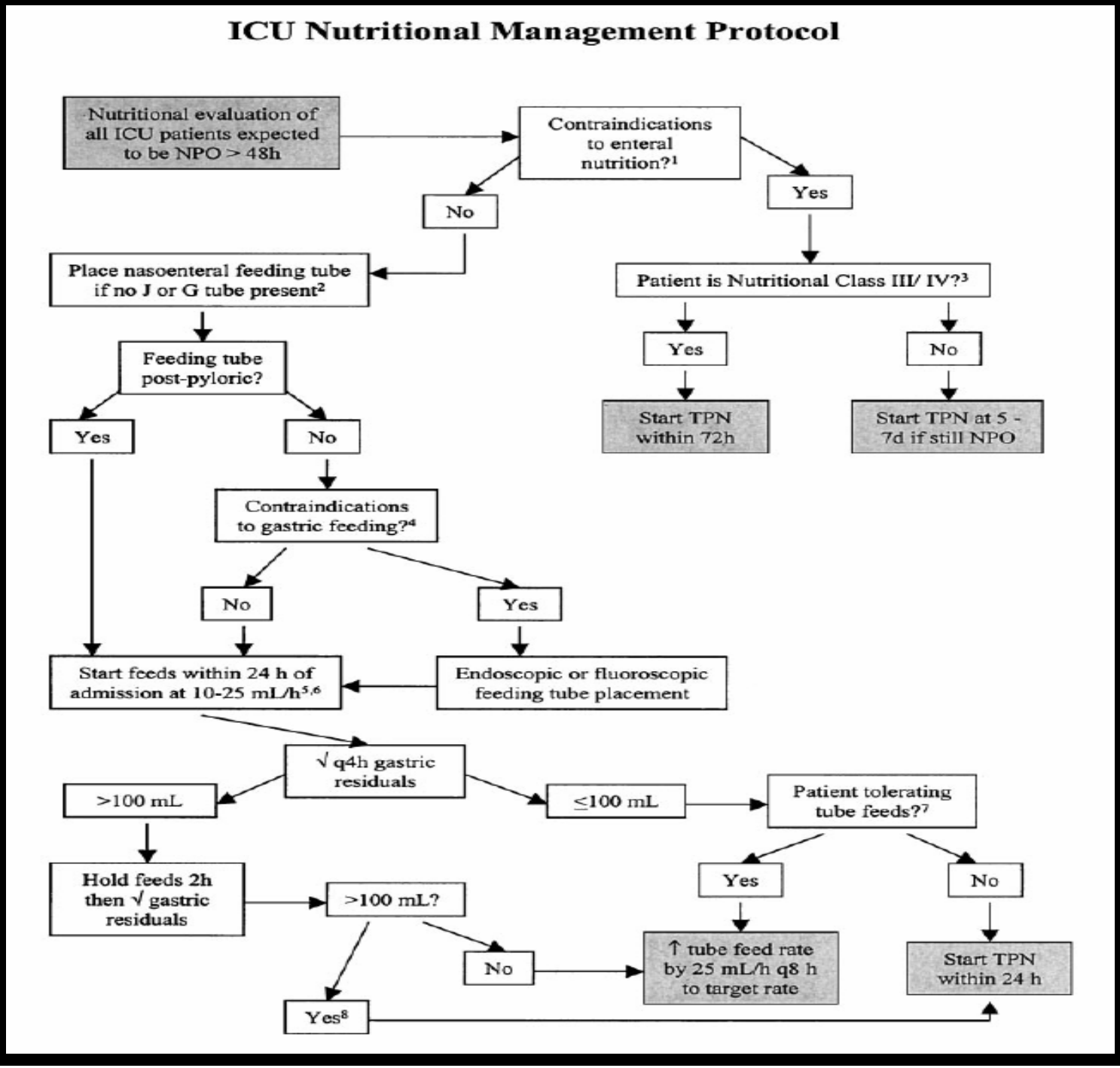
Martin CM et al CMAJ 2004; 170(2): 197-204

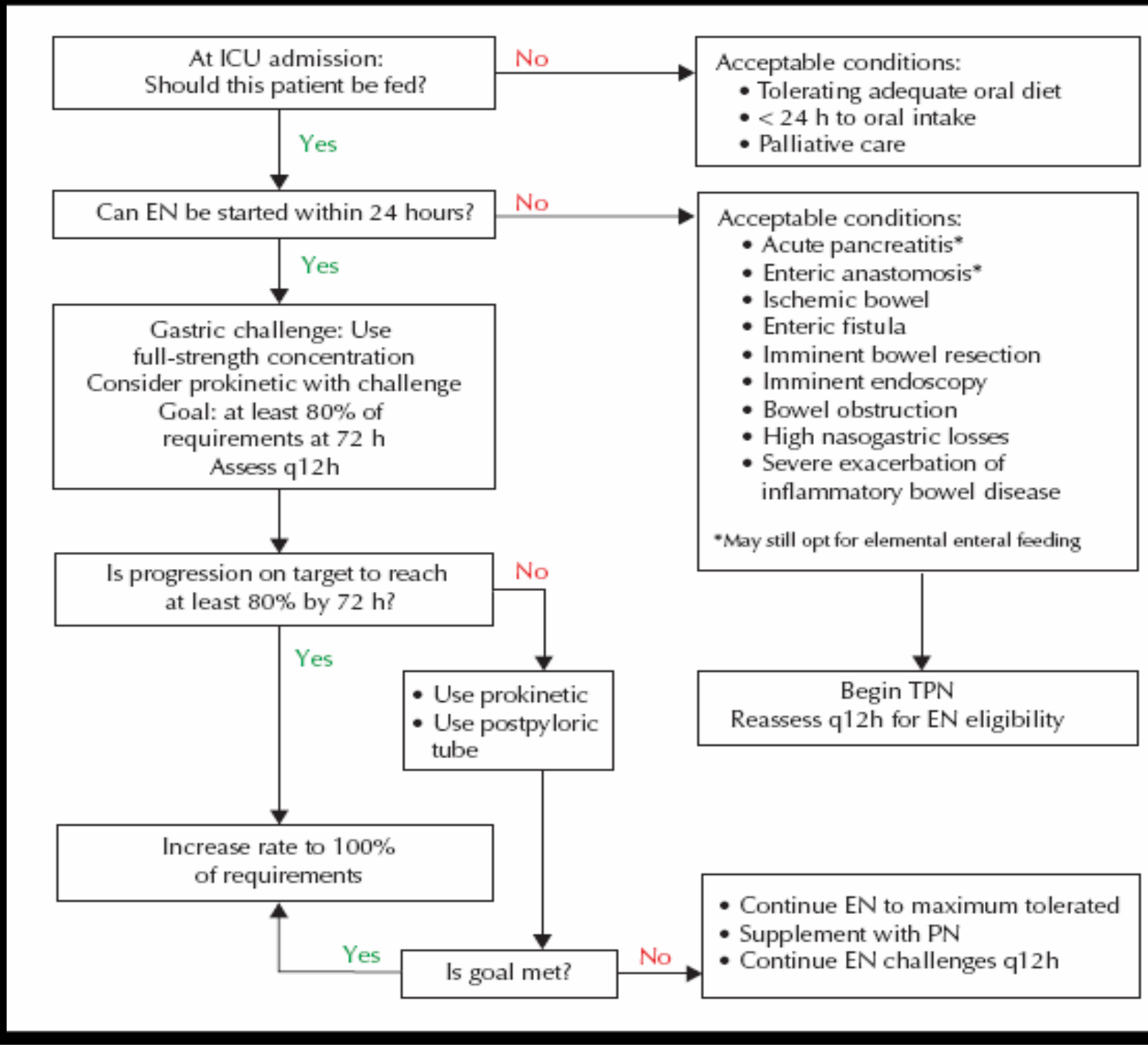
Nutrition Protocols

- Pts in intervention hospitals:
  - Received nutritional support on more no of days (EN or EN/PN)
  - Had shorter hospital LOS
  - Had reduced mortality
- No diff in:
  - ICU LOS
  - Time to initiate nutritional support
  - Total calories or protein delivered
  - No of days on which caloric goal achieved

Martin CM et al CMAJ 2004; 170(2): 197-204

ICU Nutritional Management Protocol




At ICU admission:
Should this patient be fed?
No
Acceptable conditions:
• Tolerating adequate oral diet
• < 24 h to oral intake
• Palliative care
Yes
Can EN be started within 24 hours?
No
Acceptable conditions:
• Acute pancreatitis*
• Enteric anastomosis*
• Ischemic bowel
• Enteric fistula
• Imminent bowel resection
• Imminent endoscopy
• Bowel obstruction
• High nasogastric losses
• Severe exacerbation of inflammatory bowel disease
*May still opt for elemental enteral feeding
Yes
Gastric challenge: Use full-strength concentration
Consider prokinetic with challenge
Goal: at least 80% of requirements at 72 h
Assess q12h
Is progression on target to reach at least 80% by 72 h?
No
Yes
• Use prokinetic
• Use postpyloric tube
Begin TPN
Reassess q12h for EN eligibility
Increase rate to 100% of requirements
Yes
Is goal met?
No
• Continue EN to maximum tolerated
• Supplement with PN
• Continue EN challenges q12h

Nutrition Protocols

Q: What if nutritional protocols are not established?

A:

- Daily assessment of whether a pt can be fed, in what way (EN/PN/mixed) and how much?
- All health care professionals involved in care of ICU pts (physician, nurse, dietician, physiotherapist etc) should be involved in Mx of nutritional support even when their levels of interest and knowledge widely differ

Preiser JC et al. Crit Care Med 2004; 32(11): 2354-2355.

Summary

- Nutrition is a very imp aspect of pt care in ac & ch critical illnesses
- Use of appropriate nutritional support is cost effective by reducing complication rates & duration of stay
- EN confers an enormous financial advantage over PN
- Optimal nutritional support to prevent & Rx nutritional deficiencies should become part of routine Mx of ICU pts