Nutrition & Wound Healing:
Practical Steps for Successful Assessment & Treatment

David G. Binion, MD
Professor of Medicine, Clinical and Translational Science
Co-Director, IBD Center
Director of Translational IBD Research
Director, Nutrition Support Service
Medical Director, Intestinal Rehabilitation and Transplant Center
UPMC Presbyterian Hospital
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA
binion@pitt.edu

Outline: Nutrition and Wound Healing

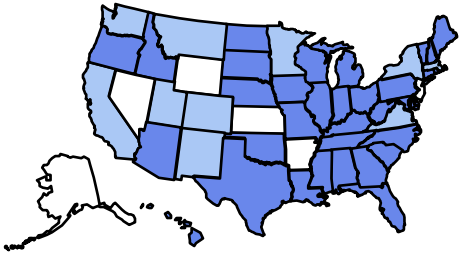
1. Changing spectrum of nutrition and malnutrition
2. Anatomy and nutritive physiology of the GI tract; Fluid shifts, digestion
3. Nutrition assessment and identification of malnutrition
3. Nutrition when the gut is available:
   Enteral nutrition support; POLYMERIC vs. ELEMENTAL feeding
4. Nutrition support when the gut is no longer available:
   Parenteral nutrition: Central venous access, TPN
5. Special considerations

Obesity Trends* Among U.S. Adults

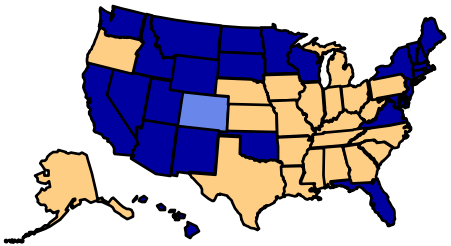
BRFSS, 1990, 2000, 2010

(*BMI ≥30, or about 30 lbs. overweight for 5’4” person)

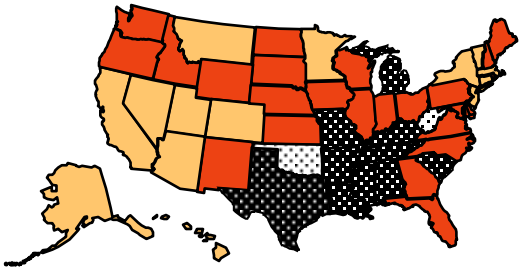
1990

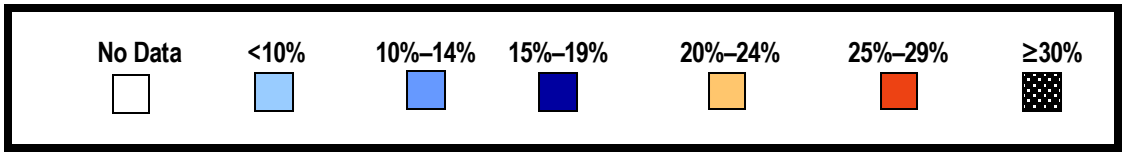


2000



2010

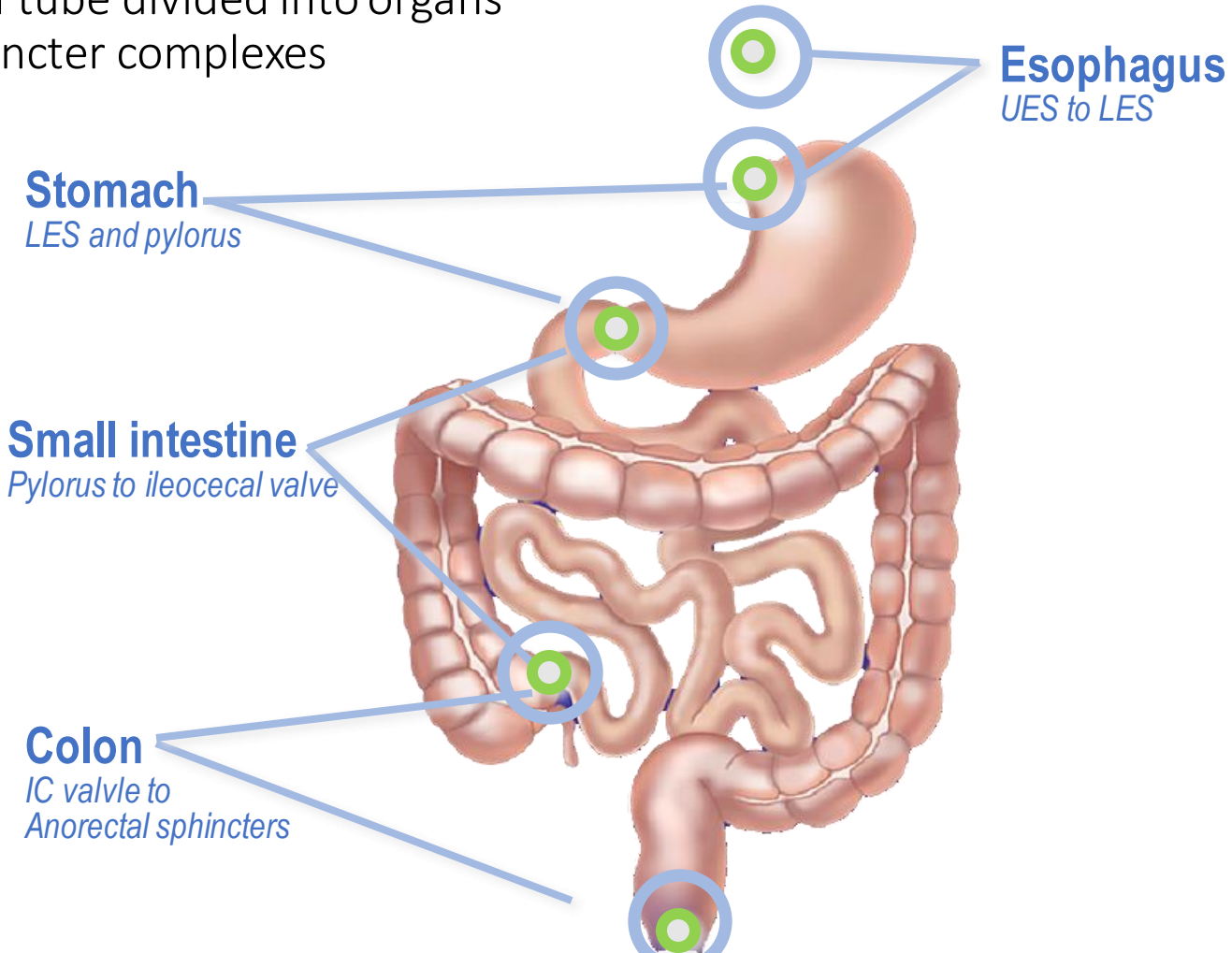




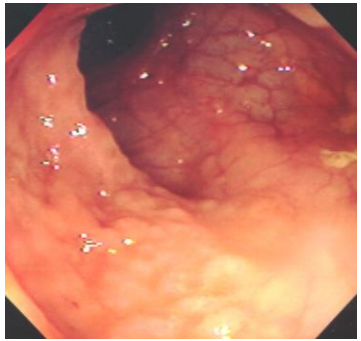
Paradox of Obesity and Malnutrition:

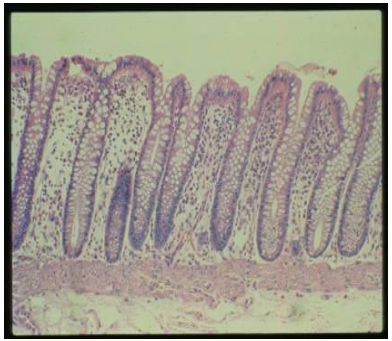
All of these individuals are at risk for malnutrition and poor medical/surgical outcomes

GI tract is a tube divided into organs with 5 sphincter complexes



The GI Tract …..
Not just a tube!





Normal GI mucosa

Surface area with external environment

As many nerves as the spinal cord

Largest immune organ in body

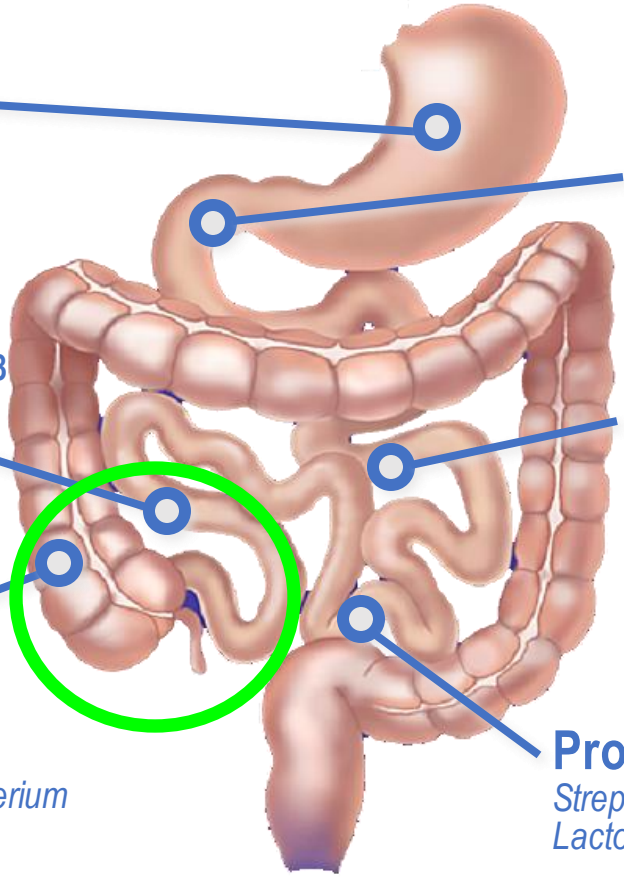
Physiologic inflammation

Oral tolerance

"You are only 10% human"

Dominant Gastrointestinal Bacteria in Normal Humans

Enteric bacteria – trigger for Inflammation and malnutrition



Stomach $0\text{-}10^2$
Lactobacillus
Candida
Streptococcus
Helicobacter pylori
Peptostreptococcus

Duodenum 10^2
Streptococcus
Lactobacillus

Distal Ileum $10^7\text{-}10^8$
Clostridium
Bacteroides sp
Coliforms

Jejunum 10^2
Streptococcus
Lactobacillus

Colon 10^{11}
Bacteroides
Bifidobacterium
Clostridium coccoides
Clostridium lepium/fusobacterium

Proximal Ileum 10^3
Streptococcus
Lactobacillus

Fluid Shifts in the Gastrointestinal Tract:
Proximal Secretion, Distal Reabsorption

Enteric fluid and high output fistula

Diet
1 - 2 liters per day

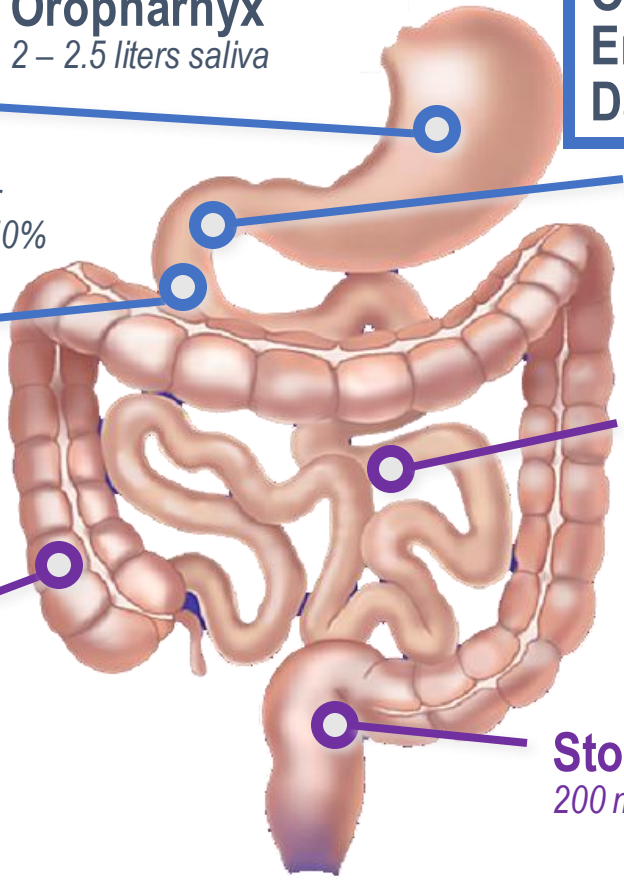
Oropharnyx
2 – 2.5 liters saliva

Over 10 liters Enters GI tract Daily

Stomach
1.5 – 2 liters Secretion
Proton pump inibitors and/or
H2 blockers can reduce by 50%

Duodenum
2 liters
Bicarbonate rich fluid

Bile
300 ml
After cholecystectomy
500 ml



Small bowel reabsorption
> 9 liters

Large bowel reabsorption
> 800 ml

Cecum
Receives 1 liter of
Fluid daily

Ileostomy should be
1 liter or less per day

Stool output
200 ml

Digestion occurs in the duodenum with pancreatic enzymes and bile

Bile contributes to impaired wound healing and fistulae

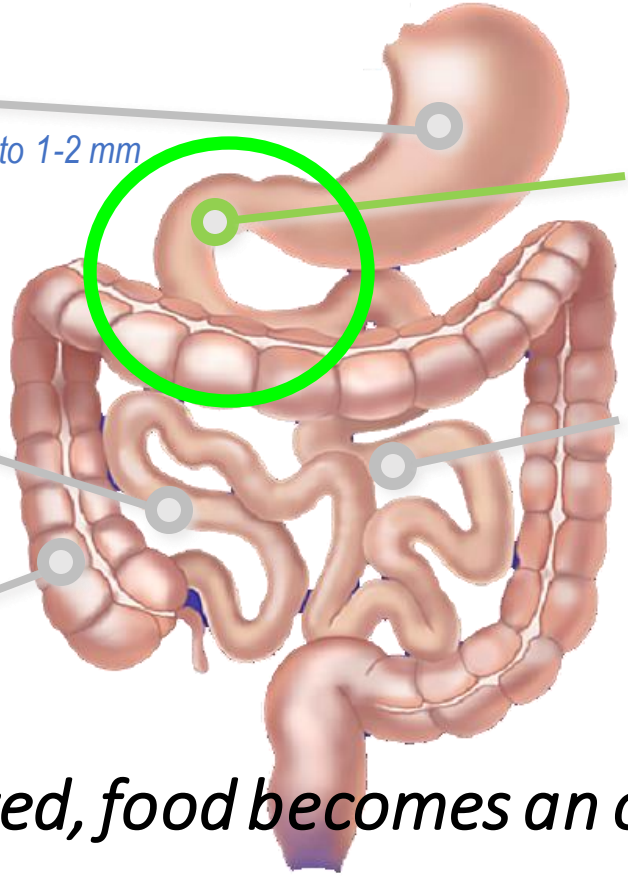
Stomach
Storage of food in the body
Antrum – grinding of food into 1-2 mm particles

Duodenum
Digestion with enzymes and bile
Absorption of iron

Distal Ileum
Absorption of bile, fat, Vitamin B12, Fat soluble vitamins (Vit A, D, E, K)

Jejunum + Ileum
Absorption of 90% of fluids, nutrition

Colon
Fluid absorption



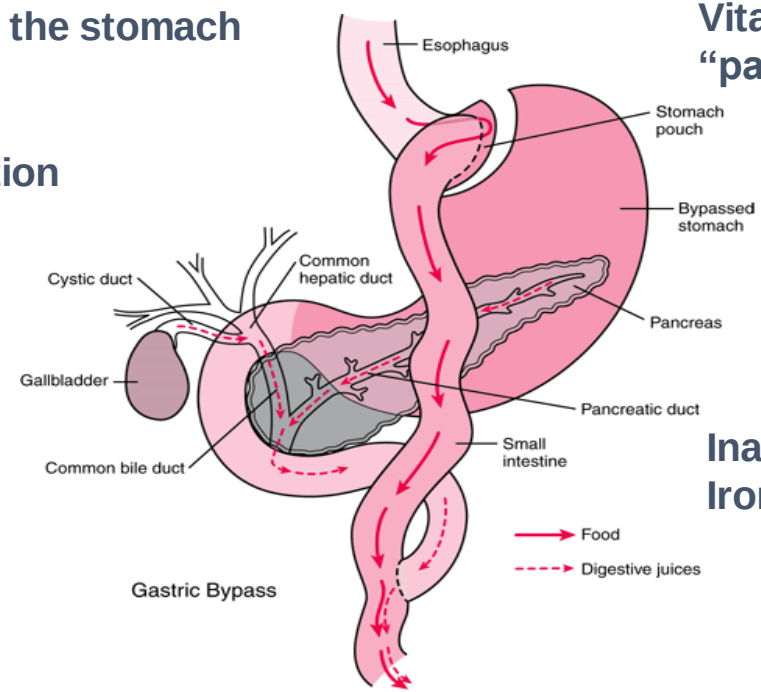
If digestion is impaired, food becomes an osmotic laxative

Roux-en-Y Gastric Bypass:
Deliberately Causing Malnutrition to Achieve Weight Loss

Food bypasses the stomach and duodenum

Impaired digestion

Inability to absorb Vitamin B12 and subsequent "pan-hypovitaminosis"



Inability to absorb Iron (no gastric acid)

Figure: The Merck Manual. *Bariatric Surgery*. Last full review/revision March 2013 by Ashish C. Sinha

Malnutrition

- Includes extremes of *Underweight* (PEM) and *Overweight* (Obesity)
- Frequent component of acute and chronic illness
- Affects > 50% of hospitalized patients
- Contributes to increased morbidity and mortality
- Nutrition assessment by a dietician within 24-48 hours of admission is a Quality Metric

- Unintentional weight loss of > 10% UBW within
- preceding 3 months
- Body weight < 90% of ideal (IBW) for height
- Body mass index (BMI) < 18.5

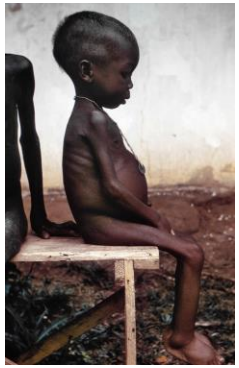
BMI = Weight (kilograms) divided by Height (square meters)

Table 3. Prevalence of Malnutrition.

Types of Patients in the Intensive Care Unit	Prevalence of Malnutrition
Heterogeneous group[8,20,21,23,26-32]	37.8%–78.1%
Elderly[34]	23.2%–34.4%
Cardiac surgery[22]	5.0%–20.0%
Liver transplantation[26,27]	52.6%
Acute kidney injury[39]	82.0%

Lew, CCH, et al. J Parenteral Enteral Nutrition. 2017; 41: 744-758.

Body Weight - Associated Disease Risk:
"U Curve" with Increased Risk at BMI Extremes



Weight Class	BMI (kg/m^2)	Risk
Extreme underweight	≤ 14.0	Extremely High
Underweight	14.1 - 18.4	Increased
Normal	18.5 - 24.9	Normal
Overweight	25.0 - 29.9	Increased ?
Obesity		
I	30.0 - 34.9	High
II	35.0 - 39.9	Very high
III	≥ 40.0	Extremely high

Starvation: Metabolic Changes

Decrease energy expenditure
Increase use of adipose tissue triglycerides (TGs) as fuel
Decrease brain glucose requirements
Maintain glucose delivery to glucose-requiring tissues
Conserve body nitrogen

Organ Function Changes in Starvation:
Physiologic "hibernation"

General: ↓ R.E.E., ↓ physical activity, ↓ body te T^o

Cardiovascular →: ↓ C.O., ↓ BP, ↓ HR

Renal: ↓ U.O., ↓ GFR, ↓ response to ADH

Pulmonary: ↓ ventilation, ↑ infections,

Gastrointestinal →: ↓ villus height, ↓ lactase

Immune: ↓ DCH (anergy), ↑ predisposition to infection

Body Composition: ↑ Na^+, H_20 retention

↑ EC H_20, ↓ IC H_20

↓ K+, ↓ Mg^{++}

↓ body fat, ↑ fatty liver

Nutrition Assessment – The "A,B,C,D's"

- Determine who is at nutritional risk
- Provide a means to monitor effectiveness of nutritional support

- ANTHROPOMETRIC measurement of body composition
- BIOCHEMICAL measurement of serum protein, micronutrients, metabolic parameters
- CLINICAL assessment of altered nutritional requirements and social psychological issues affecting intake
- DIETARY intake measurement

Clinical manifestations vary widely and depend on:

- Age of patient
- Degree of energy deficit or energy level
- Length and duration of deficiency
- Metabolic stress
- Psychosocial stress

Objective markers of nutritional assessment:

- **Clinical markers of nutritional assessment**
  - Percent ideal body weight (IBW)
  - Hand grip strength
  - Percent usual body weight (UBW)
  - Mid-arm muscle circumference
  - Serum albumin

Anthropometric Measurements

- Estimate body composition or body energy stores
- Triceps skin fold (TSF)
  measures body fat stores
- Mid-arm muscle circumference (MAC, MAMC)
  measures body protein stores

Nutrition History

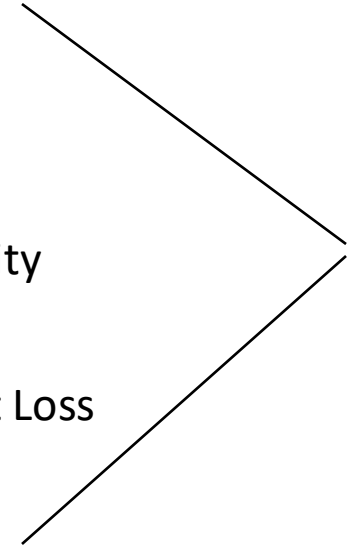
- Usual BW (UBW) vs. ideal BW (IBW)
- Actual BW (ABW)
- Percent UBW (% UBW) or deviation from UBW
  (*most sensitive marker of recent weight loss)

Biochemical Measurements

Serum	Urine
• Albumin	3-Methylhistidine
• Prealbumin	Creatinine
• Transferrin	

Subjective Global Assessment of Nutrition Status (SGA) Features

- History
- Weight Change
- Dietary Change
- GI Symptoms
- Functional Capacity
- Physical
- Subcutaneous Fat Loss
- Muscle Wasting
- Edema / Ascites



SGA Rating

___Well nourished

___Moderately malnourished

___Severely malnourished

Global Leadership Initiative on Malnutrition (GLIM) Criteria for the Diagnosis of Malnutrition

Phenotypic Criteria

- Weight loss (%): >5% within past 6 months, or >10% beyond 6 months
- Low body mass index (kg/m2): <20 if < 70 years, or <22 if >70 years. Asia: <18.5 if < 70 years, or <20 if >70 years
- Reduced muscle mass[a]: Reduced by validated body composition measuring techniques

Etiologic Criteria

- Reduced food intake or assimilation[b,c]: ≤50% of ER > 1 week, or any reduction for >2 weeks, or any chronic GI condition that adversely impacts food assimilation or absorption
- Inflammation[d,e,f]: Acute disease/injury or chronic disease-related

Diagnosis of malnutrition: Requires at least 1 phenotypic criterion and 1 etiologic criterion.

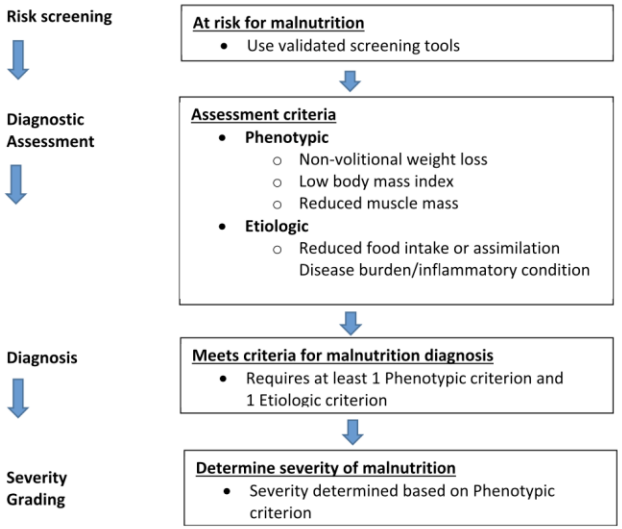


Fig. 1. GLIM diagnostic scheme for screening, assessment, diagnosis and grading of malnutrition.

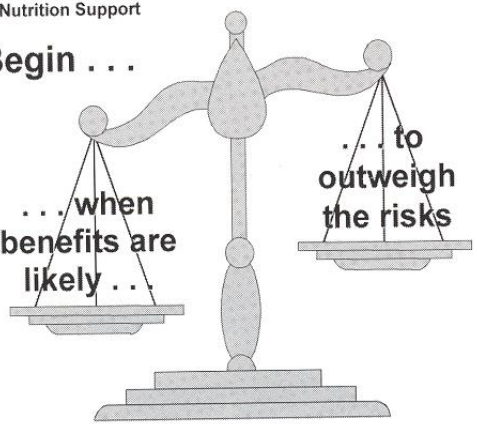
Abbreviations: GI, gastro-intestinal, ER, energy requirements.

Cederholm T, et al. Clinical Nutrition (2018), https://doi.org/10.1016/j.clnu.2018.08.002

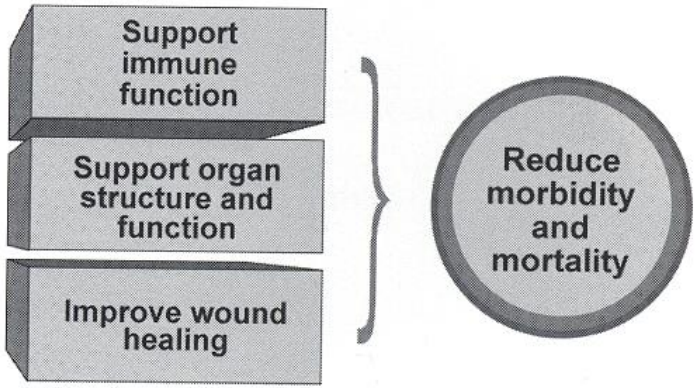
The Inpatient Dietician Clinical Nutrition Evaluation

TABLE 85.3	COMPONENTS OF A CLINICAL NUTRITION EVALUATION
Review and evaluate anthropometric measurements Review and evaluate biochemical measures Obtain and evaluate diet history and/or 24-h diet recall and/or food frequency questionnaire Conduct nutrition-focused physical examination Calculate energy, protein (and other macronutrients for patients receiving parenteral nutrition), fluid, and micronutrient requirements Determine optimal route for nutrition support (i.e., oral, enteral, or parenteral) Develop implementation and monitoring plan	

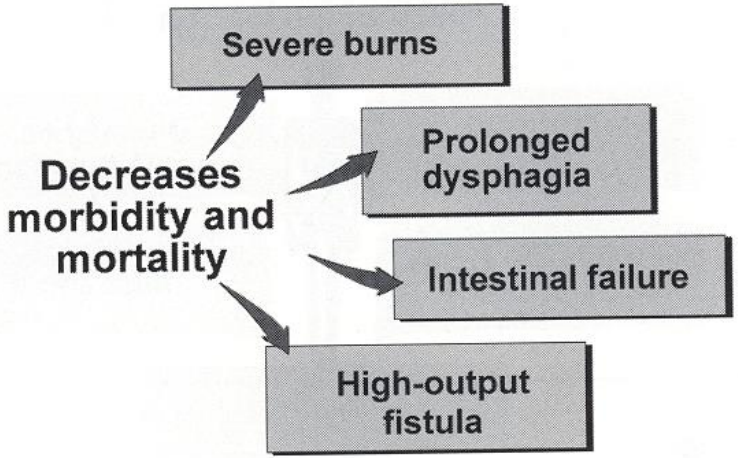
Specialized Nutrition Support



Nutrition Support Goals



Specialized Nutrition Support



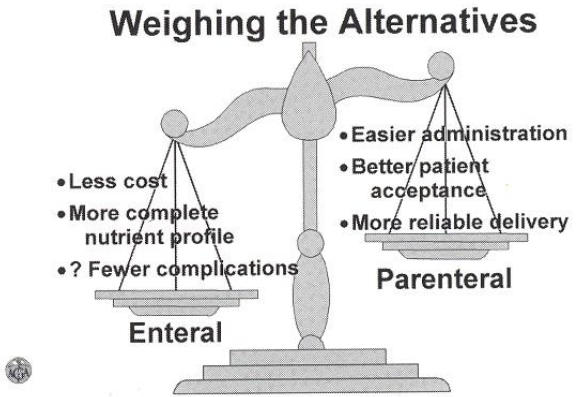
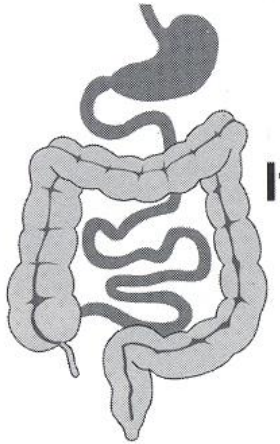


TABLE 85.1 INDICATIONS FOR PARENTERAL NUTRITION

Inability to use GI tract for >7–10 d (3–5 d in the ICU)
Diffuse peritonitis
Enterocutaneous fistula where enteral feeding is not possible
GI ischemia
Intestinal obstruction
Intractable vomiting
Intractable diarrhea
Intestinal failure
Prolonged ileus
Severe exacerbation of inflammatory bowel disease
Severe GI bleeding
Severe pancreatitis after failed EN trial
Severe malabsorption with intolerance to EN or failed EN trial
Severe malnutrition with inability to use EN

EN, enteral nutrition; GI, gastrointestinal; ICU, intensive care unit.



If the gut works . . .

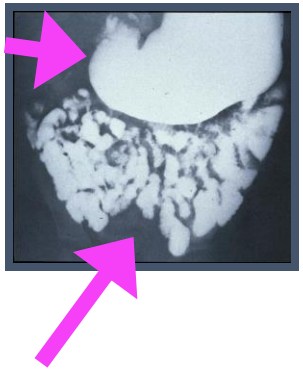
. . . Use it!

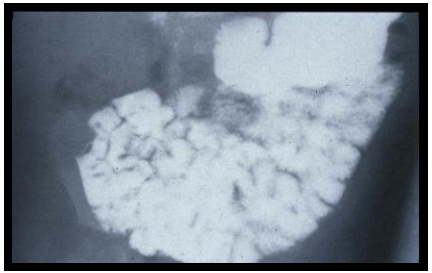
TABLE 85.2 INDICATIONS FOR ENTERAL NUTRITION

Inadequate oral intake for >7–10 d (3–5 d in the ICU) with functional gastrointestinal tract
Enterocutaneous fistula (if feeding tube can be inserted distal to the fistula)
Head or neck cancer
Inadequate oral intake to meet a high metabolic demand (e.g., trauma or burn patient)
Significant malnutrition with inadequate oral intake for repletion
Stroke or other neurologic compromise with significant dysphagia
Swallowing disorders

ICU, intensive care unit.

GI Tract: Marasmic Kwashiorkor





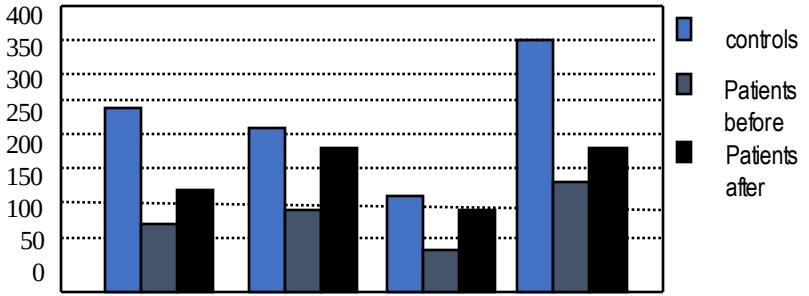
Bowel wall edema (anasarca)

Impaired motility (gastroparesis)

Impaired nutritive function

Marasmic Kwashiorkor
1 month post treatment

Malnutrition impairs digestive enzyme production:
Challenge for malnourished gut to process food



Winter TA et al. Eur J Gastro Hepatol 2000; 12(2) 191-196

Polymeric liquid nutrition: “Blended food”

Better palatability, but requires intact pancreatic function to digest prior to absorbing nutrition

Better tolerated by healthy mucosa

Many can be taken orally, as well as via tube delivery

Elemental liquid nutrition: “Predigested”

Compensates for decreased pancreatic function, compromised mucosal function (bowel anasarca).

Often requires placement of a tube, due to palatability

Newer products can be taken orally

Clinical Indications for PN

- Small bowel resection (Short Bowel Syndrome)
- Intestinal Pseudoobstruction (Systemic Sclerosis)
- Enteric Malabsorption (acute/chronic radiation damage)
- Enterocutaneous fistula (small bowel to skin)
- Intestinal Obstruction
- Inability to place enteral access devices
- Enteral Nutrition has failed to nourish patient
- Others. . .

Recommended Daily Protein Intake in Hospitalized Patients

Clinical State	Protein Requirements (g/kg IBW/d)
Normal	0.8
Metabolic stress	1.0-1.5
Acute renal failure	0.8-1.0
Hemodialysis	1.2-1.4
Peritoneal dialysis	1.3-1.5
Burn patients	1.5 – 2.0
Enterocutaneous fistula	1.5 – 2.5

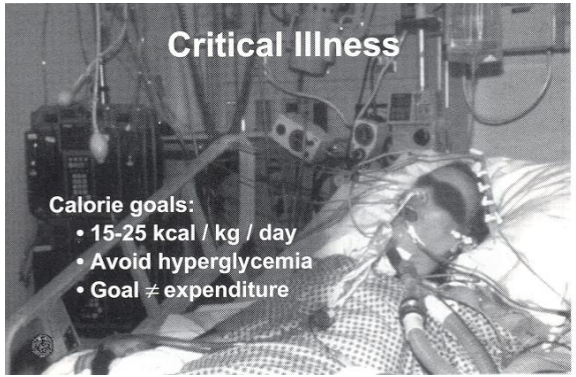


TABLE 15.5. Stepwise approach to writing a parenteral nutrition order

Patient: A 70 kg man, moderate physiologic stress

Caloric Contents of Nutrient Substances
Protein 4 kcal/g
Fat 10 kcal/g
Carbohydrates 3.4 kcal/g

Estimated Needs for This Patient

Calories	30 kcal/kg = 2100 kcal
Protein	1.2 g/kg = 84 g
Fluids	30 cc/kg = 2100 cc

Step 1—Add Protein to the PN mixture
84 g of protein needed
Each gram of protein is 4 calories (Total 326 kcal)
2100 kcal – 326 kcal = 1774 kcal still required

Step 2—Add Lipids (1.0 g/kg/day)
70 g fat = 700 kcal
1774 residual calories – 700 kcal = 1074 calories

Step 3—Add Carbohydrates
1074 kcal/3.4 cal/g carbohydrate = 295 g

Step 4—Make Total Volume
30 cc/kg = 2100 cc

Additional Additives
Electrolytes, minerals, vitamins added (See PN example formula for details)
Drug additives: histamine-2 blockers, insulin, heparin

Prevent Overfeeding!
Total Energy Expenditure (TEE)

Resting energy expenditure (REE) approximately 70% of TEE
- ↓by 15-20% with malnutrition
- ↑by metabolic stress, rarely >50%

Thermic effect of food approximately 8-10% ingested calories

Physical activity

Indirect Calorimetry

Measures respiratory quotient (how food and fuels are burned)

RQ=CO_2 eliminated/O_2 consumed

Direct measure of energy needs at rest (REE)

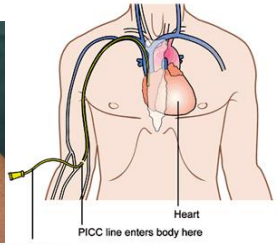
Net RQ	Substrate/Condition
≥ 1.0	lipogenesis / overfeeding
= 0.85	mixed substrate oxidation
≤ 0.7	fat oxidation/underfeeding

Overfeeding Complications

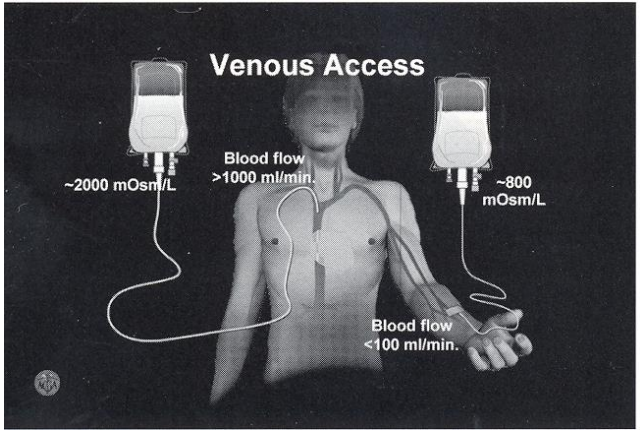
- Hyperglycemia
- Hyperlipidemia
- Fluid overload
- Increased metabolic rate
- Increased work of breathing
- Fatty liver

Choosing the best central access

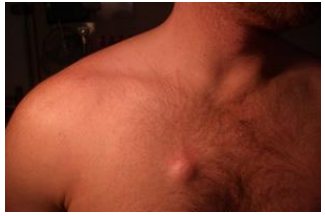
- PICC – most common, but increased risk of upper extremity DVT
- Two ports – twice the number of flushes (infections)
- One hand is not available to manipulate

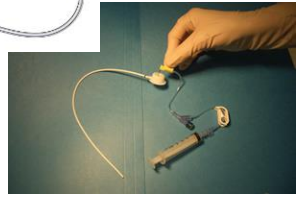


- Tunneled subclavian catheter (Hickman)
- Single lumen (dedicated for TPN)
- Both hands available to manipulate
- Silicone catheter for alcohol lock (ostomates)
- Alcohol caps on the luer lock hub(s)



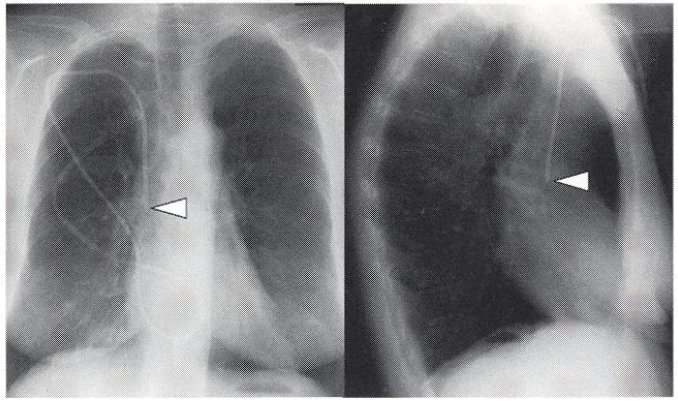
- Implantable vascular access device (i.e. Port-a-cath; Mediport)
- Indwelling (covered by skin)
- Access with Huber needle, GripperMicro needle
- Ideal for occassional/sporadic access





Complications

- Catheter related
  - Mechanical
  - Infectious
  - Thrombotic
- Hepatobiliary disease
- Bone disease
- Decreased glomerular filtration rate
- Trace element and vitamin abnormalities



Management of Line Infection

Remove line

- *Staphylococcus aureus*
- Candida
- Gram negative bacilli
- Sepsis
- Subcutaneous infection

Treatment without removal

- Antibiotic through all ports
- Urokinase
- Antibiotic lock for prevention

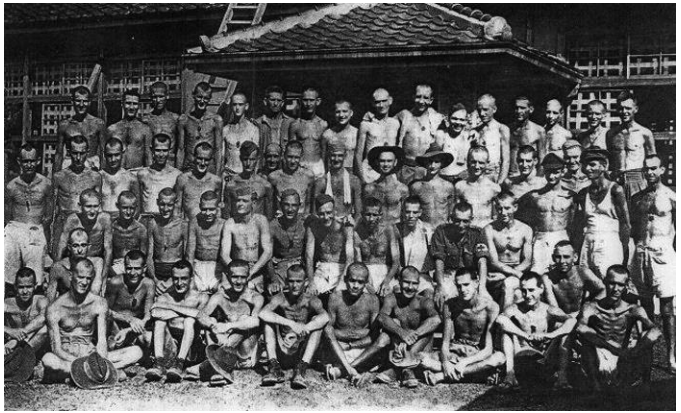
Central Line Infections

- *Staphylococcus* epidermidis
- *Staphylococcus aureus*
- Candida

- Gram-negative bacilli

Refeeding Syndrome

- Rapid worsening of hypokalemia, hypomagnesemia, hypophosphatemia with reintroduction of food (carbs)
- Sodium and water retention
- Subclinical vitamin deficiencies
- Organ failure (heart, lung)
- Cardiac arrhythmias
- Death



Australian POWs liberated at the end of World War II

Anorexia nervosa
Classic kwashiorkor
Classic marasmus
Chronic malnutrition /underfeeding
Chronic alcoholism

Morbid obesity with massive weight loss/bariatric surgery
Patient unfed for 7-10 days with evidence of stress/depletion
Prolonged fasting
Prolonged IV hydration
Phosphate-deficient TPN

1. 50% of goal kcal/protein/fluid: days 1,2
2. Vigorous repletion with IV phosphate, magnesium, potassium
3. MVI; extra Thiamine, Folic acid, Zinc
4. 75% of goal kcal/protein/fluids: days 3-7
5. Daily monitor of electrolytes, vitals (HR, T, RR) – I/O
6. Advance to goal rate at 1 week

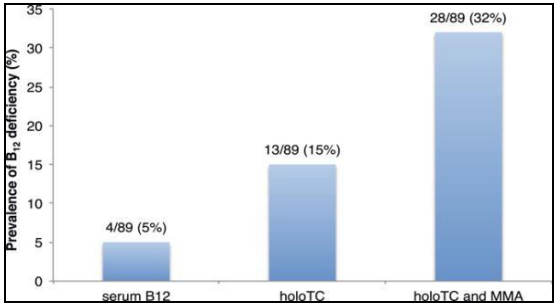
Special considerations: Vitamin B12

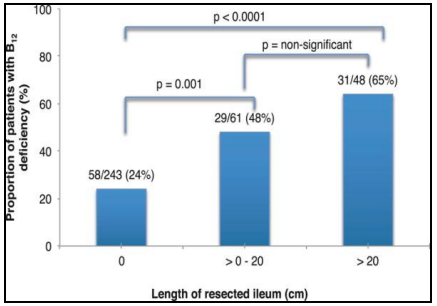
- Source - animal protein in diet
- Complex absorption – salivary haptocorrin, intrinsic factor, pancreatic exocrine function, normal motility, normal flora, terminal ileal absorption. Potential for interruption at any key step.
- Serum assay affected by acute phase response. Remember physiology of absorption – clinical suspicion of deficiency.
- Increased destruction with inflammation/nitric oxide.
- Deficiencies – megaloblastic anemia, neuropathy, enteropathy.
- Correct with injection – subcutaneous requires more frequent replacement.
- Low cost – high reward.

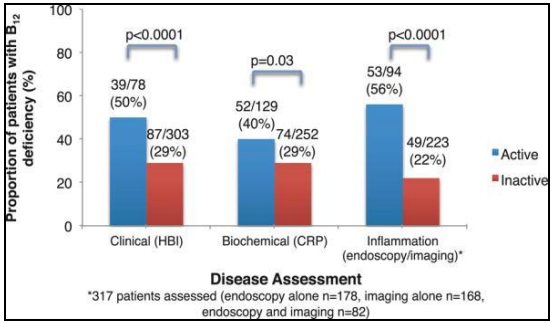
ORIGINAL ARTICLE

Prevalence and Risk Factors for Functional Vitamin B_{12} Deficiency in Patients with Crohn's Disease

Mark G. Ward, MBBS, Viraj C. Kariyawasam, MBBS,* Sathis B. Mogan, MBBS,* Kamal V. Patel, BSc, MBBS,* Maria Pantelidou, MBBS, BSc, DPMSA,* Agata Sobczyńska-Malefora, MSc, PhD,† François Porté, MBBS, BSc,‡ Nyree Griffin, MBChB, MD,‡ Simon H. C. Anderson, MD,* Jeremy D. Sanderson, MD,*,§ Dominic J. Harrington, BSc, MSc, PhD,† and Peter M. Irving, MA, MD*,§*







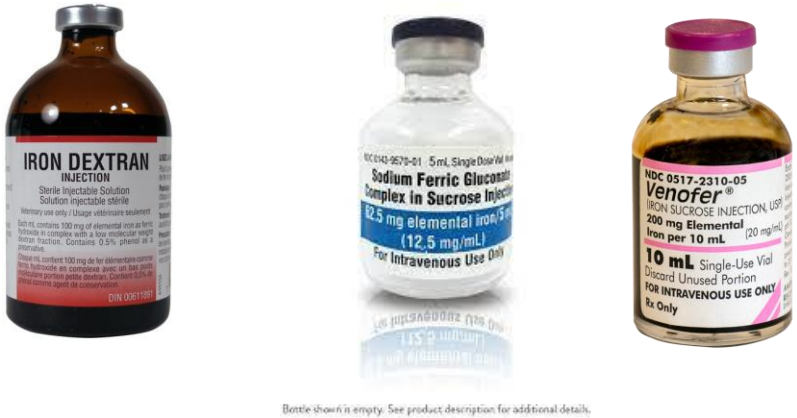
Variable	Adjusted OR	95% CI	*P*
Ileal resection			
None			
0–20 cm	3.0	1.5–6.0	0.002
>20 cm	6.7	3.0–15.0	<0.0001
Ileal inflammation	3.9	2.2–6.9	<0.0001
Active disease (HBI)	1.9	0.98–3.7	0.06

HBI, Harvey Bradshaw Index.

- 381 Crohn's disease patients and 141 UC patients
- Holotranscobalamin / MMA testing
- B12 deficiency identified in 33% of CD and 16% of UC Risks factors for B12 deficiency included:
  - ileal resection length < 20 cm: OR 3.0
  - Ileal resection length > 20 cm; OR 6.7
  - Ileal inflammation: OR 3.9
  - Imaging studies demnstrated active terminal ileal inflammation (p,0.0001) , increased disease burden (> 1 skip liesion, p,0.01, prestenotic dilatation > 3 cm, p=0.01) were associated with B12 deficiency

Special Considerations: Parenteral Iron Replacement

- Oral iron – poorly absorbed via proximal GI tract
- Potential for mucosal injury – may worsen IBD and adverse effects may cloud clinical picture
- Parenteral (IV) iron is alternative (FDA Class B for pregnancy)
- Iron dextran – original compound, requires test dose, risk of anaphylactoid reaction with infusion (including 1st administration).
- Ferric gluconate, iron sucrose – less adverse reactions; require more frequent administration.
- Ferric carboxymaltose – 750 mg single infusion but 38% with hypophosphatemia due to tubular injury.
- Iron essential for restoration of hemoglobin (oxygen delivery), cytochromes (energy generation), neuronal nitric oxide synthase (motility)



Bottle shown is empty. See product description for additional details.

“Prehabilitation”: UPMC Center for Perioperative Care

- Steven Esper, MD, MBA, Medical Director
- Jennifer Holder-Murray, MD, Surgical Director
- Systematic use of a validated risk assessment tool for patients undergoing elective procedures
- Includes nutritional assessment and intervention prior to surgery. Emphasis on high protein, liquid polymeric nutritional replacement. TPN when patients are severe.
- Avoid post-op complications and sending a patient to a nursing home/rehab facilty by using “prehabilitation” prior to the surgical procedure

Summary and Conclusions: Nutrition and Wound Healing

1. Malnutrition can occur irrespective of Body Mass Index.
2. Registered Dieticians are ready and available to provide inpatient Nutrition Assessment. Follow their recommendations!
3. Inflammation and wounds worsen nutritional status and increases protein needs
4. Consider surgically altered anatomy/physiology when developing a plan to address malnutrition in a compromised gut (i.e. need for ELEMENTAL liquid nutrition, TPN, etc.).
5. Consider nutrition intervention early – including prior to scheduled surgery with "nutritional prehabilitation" to avoid operative complications (i.e. anastomotic leaks, etc.) and need for post-op rehabilitation.
6. Use the gut when it is available with either POLYMERIC (blended food) or ELEMENTAL (predigested food) liquid nutritional feeding.
7. When the gut is no longer available, consider early parenteral support (i.e. "TPN") via central access.
8. When using TPN, be mindful of essential IV vitamin/micronutrient replacement, be vigilant to prevent and recognize refeeding syndrome, avoid over-feeding and hyperglycemia, emphasis on protein support to facilitate wound healing.