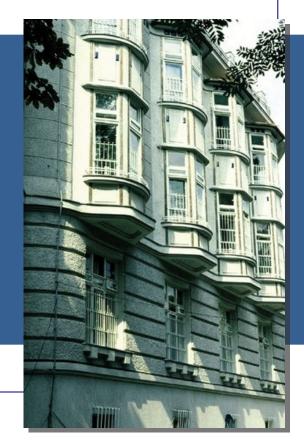
DISEASE RELATED UNDERNUTRITION

How to overcome barriers to better clinical outcome and to maximum growth?

Sanja Kolaček

Children's Hospital Zagreb



Importance of nutrition

in childhood

propriate nutritional intake is rticularly relevant to children

- high requirements for growth & maturation
- limited body reserves & rapid losses
- developmental aspects of feeding
- long-lasting consequences of malnutrition

Disease-related undernutrition

LECTURE OUTLINE

"Food is medicine, let your medicine be your food"

Hippocrates, 400 y BC

Definition, criteria, prevalence

- Influence of undernutrition on:
- ***clinical outcome**
- costs of health care
- **Causes & pathogenesis & diagnosis**
- Treatment & benefits of nutr. support

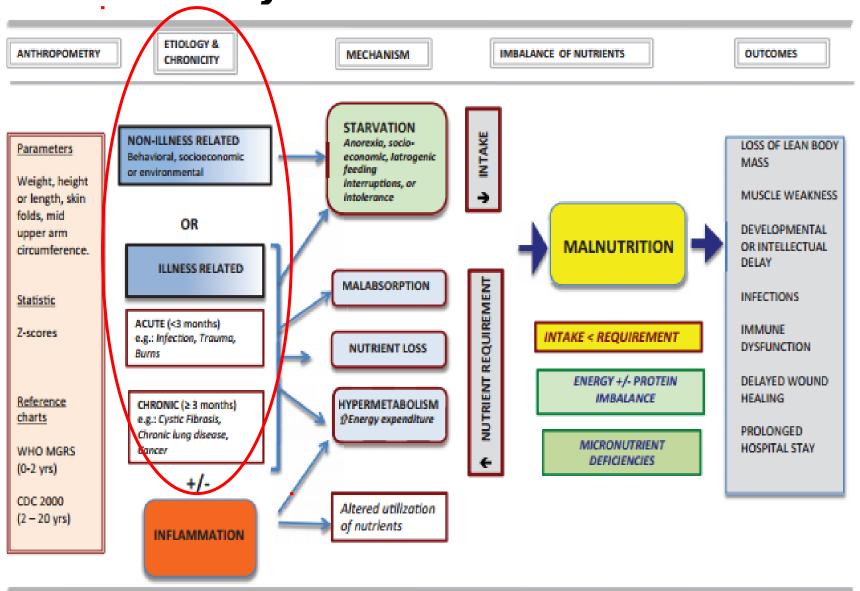
Definition of pediatric malnutrition

Mehta NM et al. JPEN 2013

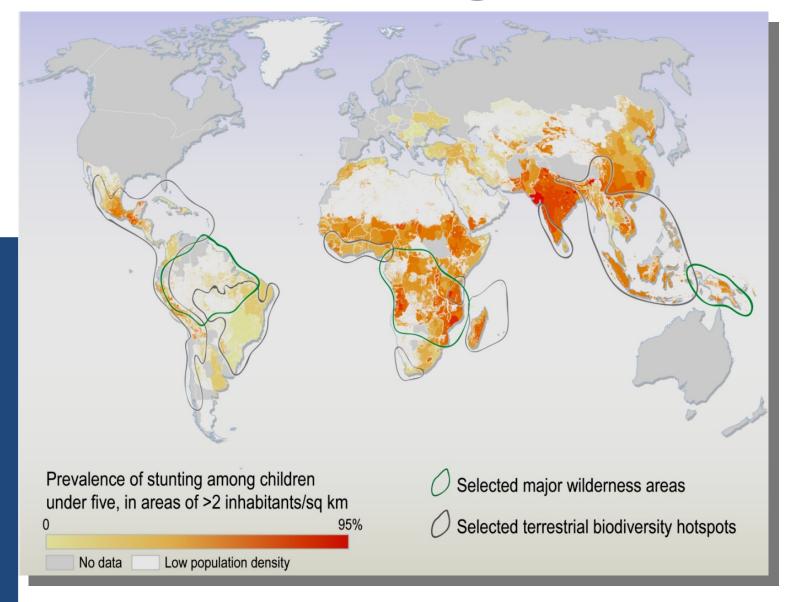
Imbalance between nutrient requirements & intake

- cumulative deficit of energy, protein & micronutrients
- negatively affects growth, development & clinical outcome

Mehta NM, et al. Defining Pediatric Malnutrition... JPEN 2013



Prevalence of stunted growth in children

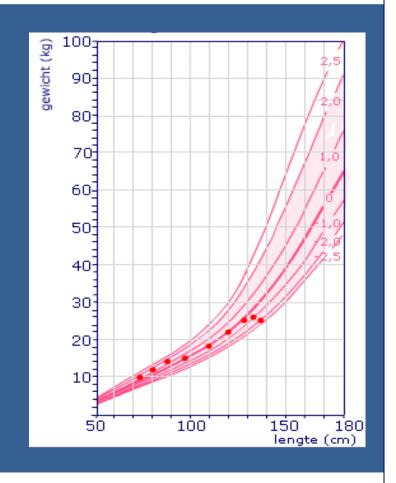


Sources: FAO 2004, Landscan 2002, Conservation International 2004

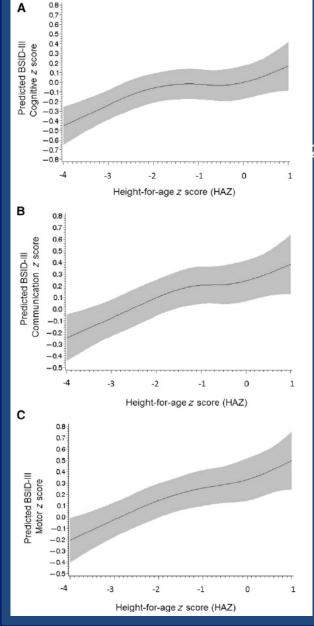
Undernutrition

LONG-TERM OUTCOME ON GROWTH

At 8 y of age, children who failed to thrive as infants - were 6 cm shorter than those who grew normally



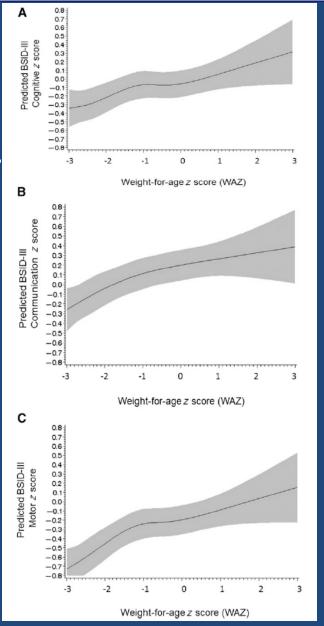
Undernutrition & cognition



Linear relation of Ht/age & Wt/age z score with cognitive, communication, and motor development in 1036 Tanzanian children 18-36m

(adjusted for age, sex, maternal education, wealth...)

Sudfeld CR et al. J Nutr 2015 (epub)



IMPORTANCE OF UNDERNUTRITION

→ 30%-50% Offmortality in children < 5y is dir or indirectly related to undernutrition

→ children with 3 indicators of malnutrition at 3y had 15.3 decrease in IQ at 11 years*

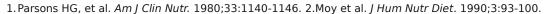
1% decrease in mainutrition

Black RE, et al. Lancet 2008, *Lio J, et al. Arch Ped Adolesc Med 2003,

CONTROL OF THE SECTION OF THE SECTION

For decades, prevalence of malnutrition remains high in hospitalized children

Report , year	Malnutrition and risk
Parsons, 1980 ¹	12% stunted; 15% wasted
Moy, 1990 ²	16% stunted; 14% wasted
Hendrikse, 1997 ³	15% stunted; 16% wasted
Pawellek, 2008 ⁴	24% malnourished
Joosten, 2010⁵	19% chronic malnutrition
Aurangzeb, 2012 ⁶	14% malnourished; 48% at risk for malnourished
Hecht, 2015 ⁷	4.0-9.3% at high risk, based on country
Chourdakis, 2016 ⁸	10-24% at high risk, based on screening tool



^{3.} Hendrikse W, et al. Clin Nutr. 1997;16:13-18. 4. Pawellek I, et al. Clin Nutr. 2008;27:72-76.



^{5.} Joosten KF, et al. *Arch Dis Child.* 2010;95:141-145. 6. Aurangzeb B, et al. *Clin Nutr.* 2012;31:35-40. 7. Hecht C. et al. *Clin Nutr.* 2015;34:53-59. 8. Chourdakis M, et al. *Am I Clin Nutr.* 2016:103:1301-1310.

Disease related undernutrition PREVALENCE Pawellek et al. Clin Nutr 2008

Table 3 Prevalence of malnutrition among paediatric patients upon hospital admission by diagnoses based on national reference data for median weight for height⁷ and cut-off points after Waterlow.⁶

Diagnosis	Malnutrition total weight for height/length <90th centile (%)	Mild malnutrition weight for height/length 81–90th centile (%)	Moderate malnutrition weight for height/length 70–80th centile (%)	Severe malnutrition weight for length/height <70th centile (%)
Patients with multiple diagnosis ($n = 32$)	43.8	21.9	18.9	3.1
Mental retardation ($n = 25$, subgroup of patients with neurological diseases)	40.0	16.0	8.0	16.0
Infectious diseases $(n = 55)$	34.5	30.9	0.0	3.6
Cystic fibrosis (CF) $(n = 12)$	33.3	25.0	8.3	0.0
Cardiovascular disease $(n = 14)$	28.6	28.6	0.0	0.0
Other non-specific diseases $(n = 26)$	28.6	11.5	11.5	3.8
Oncological diseases $(n = 22)$	27.3	18.2	9.1	0.0
Gastrointestinal diseases $(n = 110)$	23.6	17.3	6.4	0.0
Accidents $(n = 50)$	18.0	16.0	2.0	0.0
Neurological diseases (incl. mental retardation) $(n = 81)$	17.3	9.9	2.5	4.9
Respiratory diseases $(n = 15)$	13.3	13.3	0.0	0.0
Haematological diseases $(n = 8)$	12.5	12.5	0.0	0.0
Urogenital diseases $(n = 29)$	10.3	10.3	0.0	0.0
Metabolic diseases $(n = 10)$	10.0	10.0	0.0	0.0
Dermatological diseases $(n = 11)$	9.1	9.1	0.0	0.0

Disease related undernutrition PREVALENCE Cao, et al 2013

Table 2Risk category distributions of patients with different diseases.

moderate to high risk of malnutriti

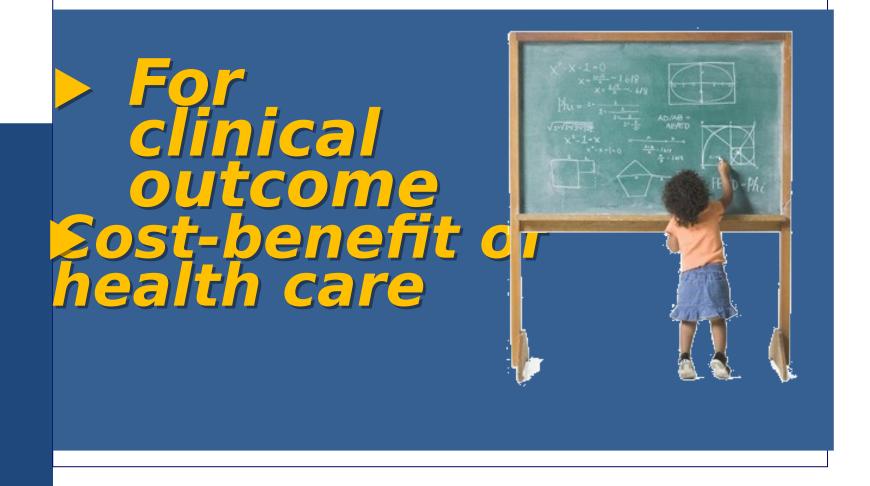
Diagnosis	Low risk (n = 630)	Moderate risk $(n = 574)$	High risk $(n = 121)$
Cardiac disease	30 (19.2%)	96 (61.5%)	30 (19.2%)
Kespiratory disease	b / (b2%)	22 (20.4%)	19 (17.6%)
Oncologic disease	39 (41.5%)	45 (47.9%)	10 (10.6%)
Gastrointestinal disease	34 (24.8%)	90 (65.7%)	13 (9.5%)
Surgery	227 (51.9%)	173 (39.6%)	37 (8.5%)
Neurologic disease	58 (58%)	38 (38%)	4 (4%)
Trauma	24 (38.7%)	36 (58.1%)	2 (3.2%)
Infection	112 (71.3%)	43 (27.4%)	2 (1.3%)
Other disease	39 (52.7%)	31 (41.9%)	4 (5.4%)

DISEASE RELATED UNDERNUTRITION

revalence: TAKE HOME MESSAGE

- Provalence is high: 10% to 30%
 - not substantially different in:
 - afluent versus less afluent European countries
 - medical versus surgical patients
 - Talence did NOT change for 30 years cors are not aware how common it is?

Does it matter if the diseased child is loosing weight??



Consequences of hospital malnutrition on clinical outcome of the disease

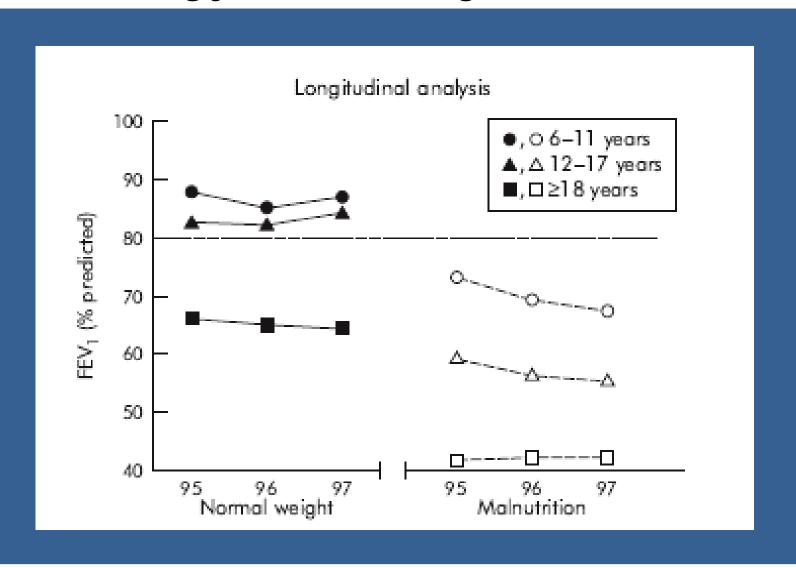
- in surgical patients
- cystic fibrosis patients
- patients with pneumonia
- oncology patients
- critically ill....

Outcome after major surgery Abdominal & thoracic in children

Secker, et al. Am J Clin Nutr 2007
175 ped. patients evaluated with SGNA
preoperatively and 30 d after surgery

- Malnourished paediatric patients had:
- significantly higher rate of infective complications
- significantly longer duration of hospitalization

Relationship between nutritional status and lung function in Cystic Fibrosis



The importance of nutrition in children with Cystic Fibrosis (CF)

ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children and adults with CF - 2016

Malnutrition is both a frequent feature & comorbidity of CF, with nutritional status <u>strongly associated</u> with pulmonary function"

→ "Nutritional management is therefore <u>standard of care in CF</u>

Turck D et al. Clinical Nutrition 2016;35:557-77

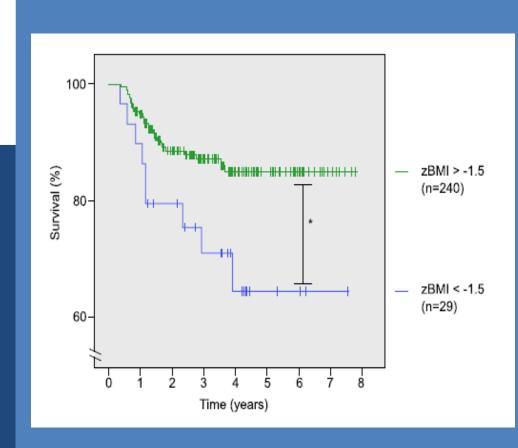
Undernutrition: negative effect on respiratory tract

In malnourished paed.patients

-Significantly higher rates of severe pneumonia (OR 4.5) (Jackson S et al. Croat Med J 2013;54)

-Significantly increased risk of death from pneumonia (OR 4.3) (Sonego M et al. PloS one 2015;10)

Consequences of undernutrition in oncology patients



- Undernutrition in initial phase of therapy is associated with worse survival in paed. cancer patients
- 2. Weight loss during therapy is associated with increased presence of febrile neutropaenia

 This underlines importance of optimal feeding in

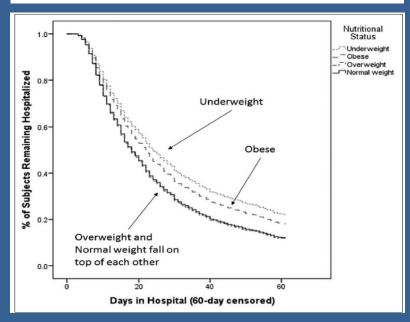
paed. cancer

Negative effect of malnutrition in critically ill

Bechard LJ et al. Crit Care Med; 2016

Clinical Outcomes Risk in Critically III Children in PICUs

OR	95% CI	P
1.53	1.24-1.89	< 0.001
1.44	0.94-2.19	0.09
1.55	0.87-2.76	0.14
1.88	1.18-3.01	0.008
1.42	0.99-2.05	0.06
1.64	1.33-2.03	< 0.001
	1.53 1.44 1.55 1.88 1.42	1.53



Participants:

1622 patients from 90 PICUs/16 countries; mean age 4.5y

Results

1.60 days mortality is 53% higher in undernourished2.Infections are more common in underweight & obese

3.Length of hospital stay signf. longer in undernourished & obese 4.Underweight patients spend significantly more days on ventilation

UNDERNUTRITION AS RISK FACTOR FOR Niseteo T, Kolaček S. Publication in process

	<u>USULI</u>	ΙΝΙΔΙ	
	Nourished patients N = 367	Malnourished patients TM/TV <- 2 SD, N = 47	þ
Gastrointestin al infections	2 - 0,62%	2 - 4,26%	0,025*
Respiratory infections	9 - 2,81%	9 - 17,02%	<0,001*
Total No. of infections	11 - 3,44%	11 - 23,4%	<0,001*

Malnourished patients have 5 x bigger risk for development of nosocomial infection

RR 5.1 (95% CI 2,276-11,485)

MALNUTRITION, LENGTH OF HOSPITAL STAY AND NOSOCOMIAL INFECTIONS

Niseteo T, Kolaček S. Publication in process

Triscico 1; Rotacek 5: 1 ubiteation in process			
	<u>Not</u> malnourished		
	Without nosocomial infection	With nosocomial infection	
Hospital stay	7,2 d (4-29)	10,2 d (6-19)	P= 0,003
	Malnourished patients		
	Without nosocomial infection	With nosocomial infection	
Hospital stay	7,9d (4-47)	15,9d (7-34)	P= 0,008

Negative financial implications of disease related undernutrition

Negative financial effect

-Patients coded as malnourished had longer hospital stay (9.7d *vs* 3.8 d)

-Significantly higher mean costs → \$ 55,255 vs \$17,309 (Abdelhadi RA. JPEN 2016)

Abdelahadi RA et al. Characteristics of hospitalized children with malnutrition..

JPEN 2016

Effect of disease-related undernutrition **SUMMARY**

- Negatively affects growth & cognitive development
- Independent risk factor for higher morbidity & mortality due to:
 - higher rate of infections
 - impaired wound healing
 - increased length of hospital stay
 - increased readmission rates
- Markedly increased cost of health care

Summarized in: Corkins MR. Nutr Clin Prac 2017;32:15-18

Disease-related undernutrition

LECTURE OUTLINE

"Food is medicine, let your medicine be your food"

Hippocrates, 400 y BC

- Definition, criteria, prevalence
- Influence of undernutrition
- on clinical outcome
- on costs of health care
- **Causes & pathogenesis & diagnosis**
- reatment & benefits of nutr. support

MALNUTRITION AS A KEY DE IOMINATOR IN THE VICIOUS CIRCLE

Acute & chronic disease

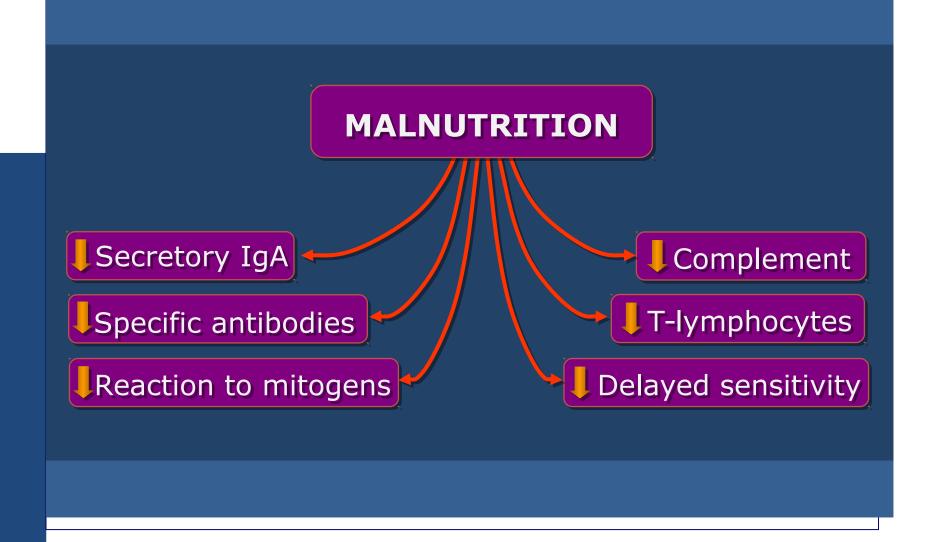
ogression of the disease quirements (inflammation ecific nutrient deficiencies due to anorexia fection utilization of nutrients mune compromise (!) absorption of nutrients

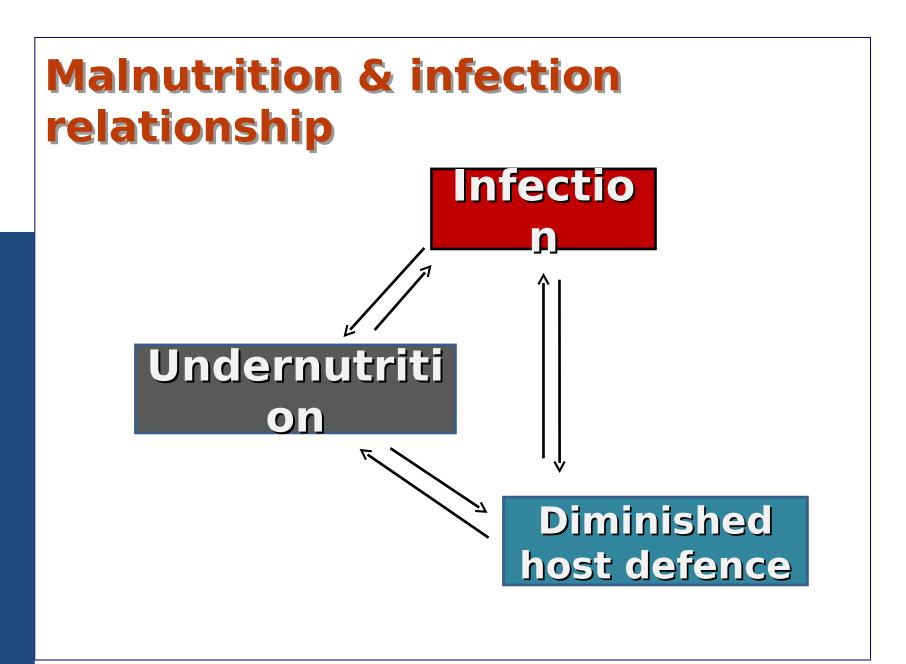




Immune deficiencies in paediatric malnutrition

(reviewed in: Cunningham-Rundles S, et al. JACI 2005; 115:1119-28)

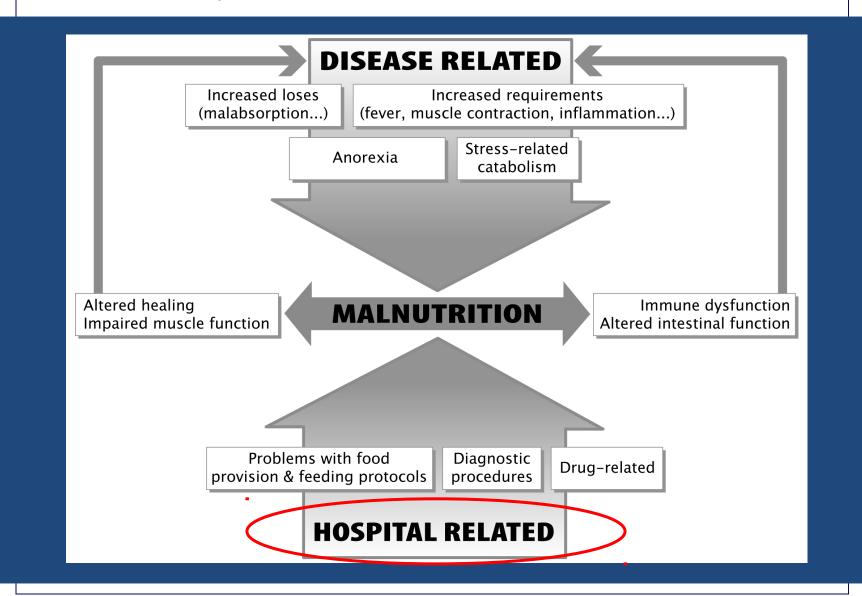




Addapted from: Calder PC, Jackson AA. Undernutrition, infection and immune function. Nutrition Research Review 2000; 13:3-29

Pathogenesis of disease-related undernutrition

(Kolaček S. 2009)



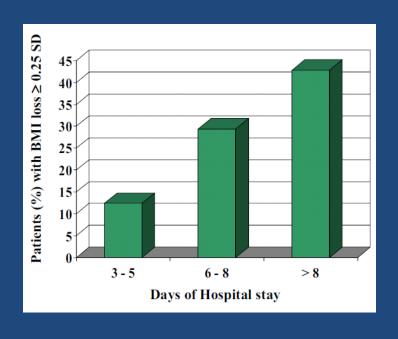
Hospital acquired undernutrition in children

In 20% to 50% of children, nutritional status deteriorates during admission to the hospital

Reviewed in: Joosten KFM et al. Clin Nutr 2014

Campanozzi A, et al.

Nutrition 2009
496 children hospitalized
due to "mild" clinical
condition
Results: the longer the stay
the higher percentage of
children with BMI
decrease \geq 0.25 SD



Etiology of hospital

La feeting practice in European hospitals

- > 5 major barriers to better nutritional care in European hospitals
 - CONSEIL DE L'EUROPE COUNCIL OF EUROPE
 - Lack of education among hospital staff
 - Lack of clearly defined responsibilities
 - Lack of influence of patients
 - Lack of cooperation among different staff members
 - Lack of involvement of hospital management/ administration

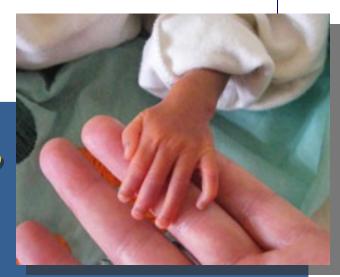
European Forum. Proceedings, Strasbourg, Council of Europe, November 2001

Disease-related undernutrition

pathogenesis

"Take home message"

- Disease related
- increased losses & requirements
- decreased intake
- Hospital related
- diagnostic procedures & therapy
- inappropriate food provision



Can we just look and diagnose un lernutrition and stunted growth?

- To measured ability of 3 experienced childcare professionals to grade nutritional status of patients of varying ages and nutritional status.
- and nutritional status.
 All patients (n=44) were in hospital for at least 3 days to enable complete assessment, and were unknown to the panel of assessors.

Can't we just look and diagnose?

Children were grouped (according to MUAC measurement) to one of 4 categories:

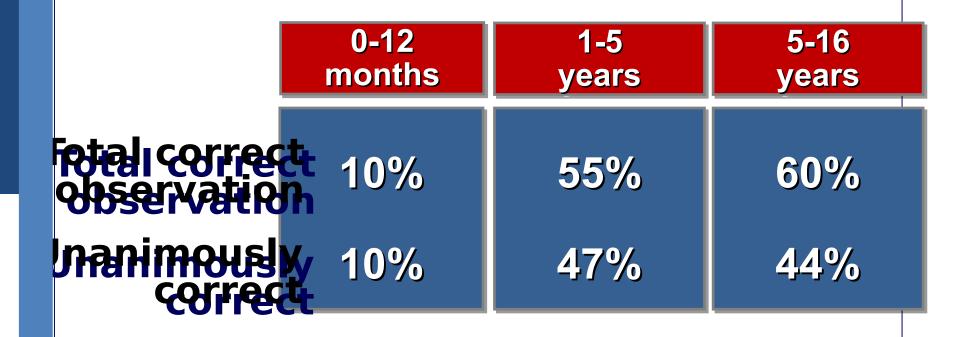
A. severe malnutrition

B. mild malnutrition

C. normal

D. obese

Percent of correct observations of nutritional status by clinical assessors classed according to age group



NO, we can't just look and diagnose, we have to do the assessment!

Nutrition assessment must be an integral part of the medical evaluation of sick children

Nutritional status should be monitored regularly in children

Disease-related undernutrition

LECTURE OUTLINE

"Food is medicine, let your medicine be your food"

Hippocrates, 400 y BC



- Influence of undernutrition
- on clinical outcome
- on costs of health care
- **Causes & pathogenesis & diagnosis**

reatment & benefits of nut. support

BASIC PRINCIPLES OF NUTRITIONAL SUPPORT

provide optimal amount of energy nutrients:

to support optimal growth & development to preserve body composition to avoid nutrition related complications to promote age-appropriate feeding habits

hould aim primarily on prevention

est approach is, the most simple one

ESPGHAN Committee on Nutrition Comment. Practical Approach to Enteral Nutrition in Children. J Pediatr Gastroenterol Nutr 2010

Nutritional Interventions in ick / Malnourished Children

Depend on:

- Age
- Clinical picture
- Possibility of oral intake
- Absorptive & digestive capacity
- Dietary habits
- Costs

Goals of treatment

of undernourished pediatric patients

- > Stages of nutritional rehabilitation are:
 - 1.To restore cellular function

short-term goal

- 2. To replete lost tissue intermediate goal
- 3. To achieve catch-up long-term goal growth

WHO Guidelines for Energy and Protein Intake for Optimal Catch-up Growth

(WHO/FAO/UNU Expert consultation. Protein and amino acid requirements in human nutrition; Vol. 935. WHO: Geneva 2007, pp. 1-265)

WHO guidelines for energy an	d protein intake for
optimal catch-up growth	

Rate of gain (g/kg/day)	Protein (g/kg/day)	Energy (kcal/kg/day)	Protein energy ratio (PE %)
10	2.82	126	8.9
20	4.82	167	11.5

Average increase in energy and protein in diseased children

(Taken from: Koletzko B. Nutritional needs of children and adolescents. In: Sobotka L, ed. Basics in Clinical Nutrition, Prague: Galen; 2011)

Condition	Clinical diagnosis	Energy (%)	Protein (%)
Healthy child	Normal population	100	100
Mild stress	Anaemia, fever, mild infection, elective small surgery	100-120	150-180
Moderate stress	Skeletal trauma, chronic disease (e.g. cystic fibrosis with dyspnea)	120-140	200-250
Marked stress	Sepsis, severe skeletal/muscular trauma, major surgery	140-170	250-300
Critical stress	Severe burn injury, quick rehabilitation after malnutrition	170-200	300-400

Management strategy

nutritional status

for disease-related malnutrition

Parenteral nutrition Enteral feeding Oral nutritional supplements Nutritional counseling Nutritional intervention should increase in stepwise manner in respects to severity of underlying condition and impairment of

Indications for PN

Reserved for patients with

- dysfunctional
- inaccessible
- **inexistent GUT**



PN compared to EN

Much more complicated

Lower safety profile

PN associated complications

(CV related sepsis & thrombosis...)

Two to fourfold higher costs

Enteral Nutrition DEFINITION DEFINITION

- Feeding directly into stomach or duodenum / jejunum over tripead stoma
- **Oral** provision of dietary foods for special medical purposes

EN in Paediatrics WHEN?

- A.
- Not growing well on oral intake + GIT function sufficiently preserved Not growing well ???
 - Growth failure >1 months in child <2 y
 - Growth failure >3 months in child >2 y

- В.
- EN used as treatment of the disease (allergy, Crohn,
- C.
- Total feeding time >4 h/day in a disabled child

EN in Paediatrics: How Diamanti A, et al. Home EN in children: a 14-year multicenter survey. Eur J Clin Nutr 2013

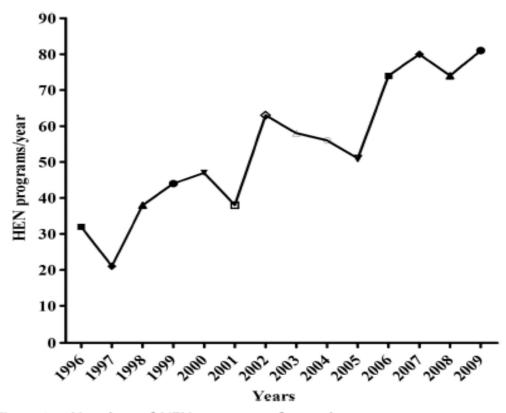
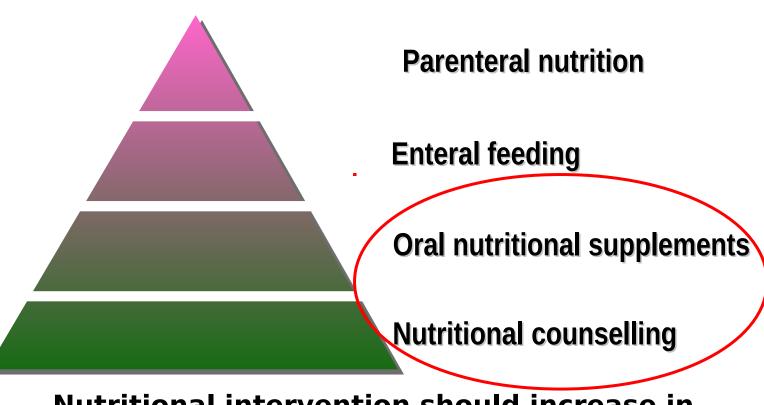


Figure 1. Number of HEN programs for each year.

757 recorded cases 1996 – 2009 on HEN
Prevalence 3.5 / 100 000, incidence 2.45 / 100 000 children 1-18y

Management strategy for disease-related malnutrition



Nutritional intervention should increase in stepwise manner in respects to severity of underlying condition and impairment of nutritional status

Management strategy Nutritional counselling

Tet children to eat more without unnecessary restriction

the simpliest, cheapest and safest nutritional support

Management strategy:

Oral nutritional supplements

dietary advice does not suffice hild is not growing well



add paediatric formula as a nutritional supplement - sip feed

ESPGHAN Committee on Nutrition Comment, JPGN 2010;51

HOW TO SELECT A TYPE OF FEED?

Selection of Formulae

Age specific nutritional requirements

infants ► small children ► adult formulae

Intestinal, liver & pancreatic function

Food intolerances or allergy

allergens, gluten, lactose, phenyl-alanine...

Formula features:

osmolality, viscosity, costs, taste

Site & route & mode of delivery

Selection of EN formulae Sandard paediatric formula

Age adapted nutritional composition: pediatric formula to be used ≤ 10-12 years of age

Is caloric (1 kcal/ml), iso-osmolar (300-350), mostly gluten & lactose free

Polymeric formula: source of nitrogen are whole peptides

Addition of fibres??

Enteral Formula Selection: addition of fibres

Elia M et al. Clinical effects of fibre containing enteral formulae - systematic review & meta-analysis. Aliment Pharmacol Ther 2008

 Significant benefit of fibre supplemented

versus unsupplemented EN formula in:

- a. patients and healthy controls
- b. predominant symptom diarrhoea & constipation

Indications to formulae in respect to nitrogen source

	POLYMERIC	SEMI- ELEMENTAL	ELEMENTAL
Nitrogen (casein, lactalb., soy)	whole proteins	small peptides	amino-acids
Carbohydrates	glucosae polymers		
Fats	LCT or LCT & MCT		
Osmolarity	300	300 - 450	300 - 600
Indications	multiple	allergy, malabsorption	multiple allergies, severe malabs.
Advantages	palatable, cheap	hypoallergenic rapid absorption	non-allergenic immunomodulatory
Disadvantages	intact GIT	bitter, expensive	expensive, bad taste, hyperosmolar

Selection of disease specific EN formulae

MCT based	requires no lipase & bileabsorbed to portal blood (not lymph)
High energy (1.3 - 2.0 kcal/ml)	fluid restrictionincreased energy requirements
High nitrogen (>15%)	catabolic patientswound healing
High lipids (>35%)	respiratory problems, high energy requir.
Addition of immunonutrients	 glutamin, arginin, n-3 FA, nucleotides, TGF-beta & probiotics, prebiotics
Other disease specific	• liver, renal, lung, diabetes

Enteral Formulae Selection

role of disease-specific formulations

- Could be beneficial in certain clinical conditions
- Good controlled studies in children are lacking

CLAIMS SHOULD BE EVALUATED CRITICALLY

Selection of appropriate enteral formula

Standard polymeric formula can be safely used in majority patients, irrespective of their basic clinical condition, but with functioning GUT.

BEST COST-BENEFIT RATIO

CLINICAL NUTRITION IN CHILDREN

EFFECT OF NUTRITION **SUPPORT** ON THE PROGNOSIS OF THE

Therapeutic effect of nutritional support in adults

```
7-11 RCT: nutr. suppplements
                          26% vs. 17%
  mortality..... 27% vs. 12%
                          28 d vs. 19 d
   complications.....
9-12 RCT: trube feeding length of
  hospitalization..... 23% vs. 11% mortality..... 48% vs. 33%
                          46% vs. 23%
   complications.....
```

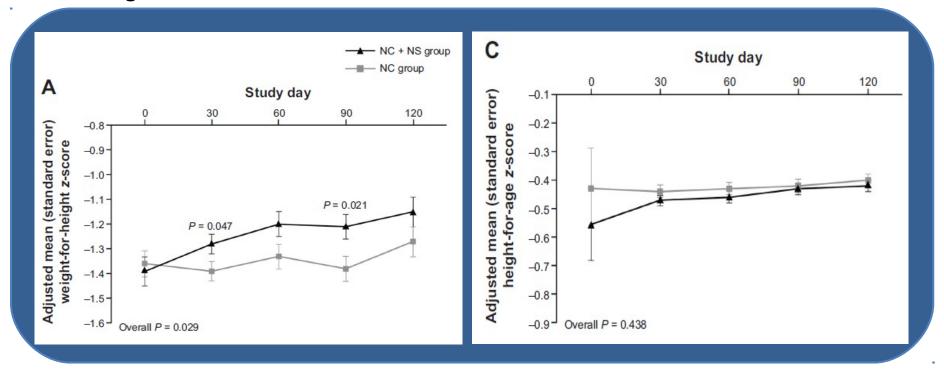
Stratton RJ, et al. Disease related malnutrition: evidence based approach. CABI Inter. 2003

NUTRITIONAL COUNSELING (NC) *VS.*COUNSELING + ORAL NUTRITIONAL SUPPLEMENTS

Sheng X, et al. Nutrition and metabolic insights 2014;7:85-94

RCT in children with picky eating, ages 30-60 months, receiving NC (n=76) or NC+ONS (n=77) for 120 days - examined at 30, 60, 90 and 120 d

- **Results:**
- 1. In NC+ONS significantly greater intake of energy, protein, omega3 FA, Ca, P, Fe, Zn, & vit A, C, D, E and B6
- 2. Wt for Ht Z score significantly greater at NC+ORS over entire period
- 3. Ht/age Z score not different



Role of nutritio support in children with CF

Lai HC et al. Pediatrics 2009

Catch-up in weight gain within the first 2y
 after diagnosis was the strongest predictor
 of lung function at the age of 6 y

 Improved lung function correlated with reduced morbidity and mortality

Nutritional care benefits neurologically impaired children

Children with neurologic impairments (such as cerebral palsy) have a lower caloric intake, altered metabolism and excessive nutrient losses. Improved

nutritional support have shown the following

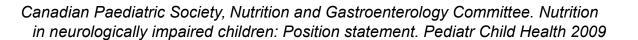
benefits:

Fewer infections and decubitus ulcers

Decreased irritability and spasticity

Less use of health care facilities

Improved quality of life





The importance of nutrition support in children with inflammatory bowel disease

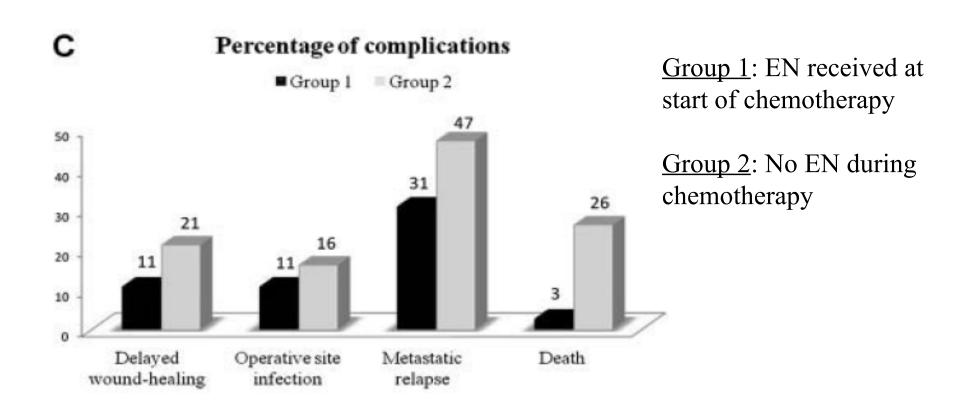
ECCO-ESPGHAN consensus guidelines on medical management of pediatric Crohn's Disease

- → Linear growth impairement is present in almost 50% of children with Crohn's disease before any other symptom of the disease appear. It is a marker of disease activity_
- → Restoration of linear growth can be considered as an indicator of good disease control and of treatment success

Staiano A et al. JPGN 2018

Tolerance and efficacy of preventive gastrostomy feeding in pediatric oncology

- (Schmitt F et al. Pediatr Blood Cancer 2012; 59:874-880)
- Preventive PEG in 74 ped. cancer patients
- If EN started at beginning of treatment final height loss lower (-0.5 vs -1.2 SD of zH/A)
- Conclusion: EN over PEG prevents malnutrition; positive oncology outcome?



Nutritional therapy is cost-effective

Study

Retrospective analysis by Lakdawalla et al. (*JPEN* 2014)

Purpose

To assess the effect of oral nutrition support (ONS) on length of stay (LOS) and hospital costs.

Participants

A total of 557,348 pediatric inpatients in 460 USA hospitals from 2000-2010.

Findings

Children with ONS had decreased LOS (1.1 d) and decreased hospital costs (\$1,768 per patient).







Disease-related undernutrition

KEY MESSAGES

- Serious impact on growth
- belevelopment Delevelopment clinical outcome

Looking for malnutrition should be integral part of paediatric care

Timely established nutritional management improves clinical outcome & is cost-effective

Forr ulae: level of protein hydrolysation

Partially hydrolysed Sigomoria oligomeric monomeric

Contain oligopeptides, Contain di- and three-Mixture of crystalline molecular mass<5 kDæeptides, very low arrino-acids molecular mass <3.0 kDa

Number of epitopes

Can cause allergic

reaction in children

owered

with CMPA

Most of the epitopes

destroyed

Tolerated by 90% of

patients with CMPA

Good taste, cheaper Bag taste, expensive No antigen sequence epitopes

Often hyperosmolar

Very expensive

Classification of pediatric malnutrition

- Mehta NM et al. JPEN 2013
- A. Due to environmental/behavioral causes
 - no inake because of food unavailability
 - no intake due to food aversion/behavioral problems
- B. Due to disease "disease-related undernutrition"

Based on duration

A.<u>Acute</u>: duration < 3 months

B.Chronic: duration > 3 months,

relevant for long-

term negative effect on growth and

development

Management strategy how to make a choice of enteral formula?

ESPGHAN recommendations

SPGHAN Committee on Nutrition. JPGN 2010;51:110-122

- should provide balanced mix of all essential nutrients - at least 100% of requirements
- nutrient composition should be age adapted
 - paediatric enteral formulae
- adult formula to be used after 10 years