### 2nd Singapore Clinical Nutrition Meeting

# Supplements to promote wound healing – Does every patient need it

R Sim Centre for Advanced Laparoscopic Surgery, TTSH





## **ESPEN** Guidelines

- Patients at risk should be given oral supplements, enteral or parenteral nutrition, and ideally immunonutrition.
- Regardless of nutritional status, patients should be given oral supplements before major abdominal surgery.











### **Normal Wound Healing**

Inflammation Injury x 4-6 days: Wound exudation and fibrin clot formation, neutrophils remove bacteria, macrophage activity

Proliferation 3-5 days post-injury x 2-3 weeks: Epithelialization, angiogenesis, fibroblast proliferation, collagen deposition and crosslinking, wound contraction

Zinc

### Remodeling

2-3 weeks post-injury x 2 yrs: Collagen maturation and stabilization, development of tensile strength Vitamin A

Vitamin C

Thompson et al, NCP, 2005;20:331-347







### Summary of risk factors for delayed wound healing:

Arthritis

- Chronic liver disease
- Diabetes
- Excess alcohol intake
- Impaired self-caring
- Inadequate nutrition
- Inflammatory disease
- Older age (over 65 years)

- Polypharmacy
- Poor circulation
- Poor cognition/cognitive dysfunction
- Renal failure
- Smoking
- Vascular disease
- Weakened immune system

## Nutrition and wound healing

- Malnourished at risk of delayed wound healing and development of chronic wounds
- When undernutrition is a/w SIRS, wound healing may be almost blocked
- Vicious cycle of chronic inflammation aggravating severity of malnutrition



#### ESPEN



### **Prevalence of Malnutrition**

- ambulatory outpatients 1-15%
- institutionalized patients 25-60%
- hospitalized patients 35-65%

#### ESPEN



#### THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND NETABOLISM

## **Screening tools**

- Nutritional Riks Index<sup>1</sup>
- Subjective global assessment<sup>2</sup>
- Malnutrition Universal Screening Tool (MUST)<sup>3</sup>
- Nutritional Risk Screening (NRS 2002)<sup>4</sup>
- MNA (elderly)<sup>5</sup>

1 Veterans Affairs, New Engl J Med 1991 2 Detsky et al, JPEN, 1984 3 BAPEN

4 Kondrup et al, Clin Nutr 2003 5 Vellas et al, Nutrition 1999

**Recommended by ESPEN** 



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## Basic nutrition principles

- Intake must cover daily requirements of energy (30-35 kcal/kg) and protein (1.0-1.5g/kg)
- Undernourished or non-healing wounds daily energy and protein intake increased to 35-40 kcal/kg and 1.5-2.0g/kg respectively
- Often such intake cannot be met in a standard diet
- Nutritional supplements must be given



### Basic nutrition principles

- Enteral whenever possible, parenteral if required
- Adequate gut function itself is an indicator of outcome
- Overfeeding is the commonest cause of feed related morbidity
- Underfeeding may actually be a/w
  reduction of septic complications and LOS



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#### ORIGINAL ARTICLE

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### Early versus Late Parenteral Nutrition in Critically Ill Adults

Michael P. Casaer, M.D., Dieter Mesotten, M.D., Ph.D., Greet Hermans, M.D., Ph.D., Pieter J. Wouters, R.N., M.Sc., Miet Schetz, M.D., Ph.D., Geert Meyfroidt, M.D., Ph.D., Sophie Van Cromphaut, M.D., Ph.D., Catherine Ingels, M.D., Philippe Meersseman, M.D., Jan Muller, M.D., Dirk Vlasselaers, M.D., Ph.D., Yves Debaveye, M.D., Ph.D., Lars Desmet, M.D., Jasperina Dubois, M.D., Aime Van Assche, M.D., Simon Vanderheyden, B.Sc., Alexander Wilmer, M.D., Ph.D., and Greet Van den Berghe, M.D., Ph.D. N Engl J Med 2011; 365:506-517 August 11, 2011 DOI: 10.1056/NEJMoa1102662



ARTICLES & MULTIMEDIA \*

Citing Articles (167)

ISSUES \*

### BACKGROUND

Controversy exists about the timing of the initiation of parenteral nutrition in critically ill adults in whom caloric targets cannot be met by enteral nutrition alone.

Full Text of Background...

### METHODS

In this randomized, multicenter trial, we compared early initiation of parenteral nutrition (European guidelines) with late initiation (American and Canadian guidelines) in adults in the intensive care unit (ICU) to supplement insufficient enteral nutrition. In 2312 patients, parenteral nutrition was initiated within 48 hours after ICU admission (earlyinitiation group), whereas in 2328 patients, parenteral nutrition was not initiated before day 8 (late-initiation group). A protocol for the early initiation of enteral nutrition was applied to both groups, and insulin was infused to achieve normoglycemia.

Enrollment and Outcomes.

#### FIGURE 2



Total Energy Levels.

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### A Randomized Trial of Glutamine and Antioxidants in Critically III Patients

Heyland, Daren M.D.; Muscedere, John M.D.; Wischmeyer, Paul E. M.D.; Cook, Deborah M.D.; Jones, Gwynne M.D.; Albert, Martin M.D.; Elke, Gunnar M.D.; Berger, Mette M. M.D., Ph.D.; Day, Andrew G. M.Sc.; the Canadian Critical Care Trials Group

#### Author Information

From Kingston General Hospital, Kingston, ON (D.H., J.M., A.G.D.), St. Joseph's Healthcare, Hamilton, ON (D.C.), Ottawa Hospital, General Campus, Ottawa (G.J.), and Hôpital du Sacré-Coeur de Montréal, Montreal (M.A.) — all in Canada; University of Colorado School of Medicine, Aurora (P.E.W.); University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, Germany (G.E.); and Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland (M.M.B.).

Address reprint requests to Dr. Heyland at Angada 4, Kingston General Hospital, Kingston, ON K7L 2V7, Canada, or at dkh2@queensu.ca.

Supported by the Canadian Institutes of Health Research.

Disclosure forms provided by the authors are available with the full text of this article at <u>NEJM.org</u>.

#### ABSTRACT

BACKGROUND: Critically ill patients have considerable oxidative stress. Glutamine and antioxidant supplementation may offer therapeutic benefit, although current data are conflicting.

METHODS: In this blinded 2-by-2 factorial trial, we randomly assigned 1223 critically ill adults in 40 intensive care units (ICUs) in Canada, the United States, and Europe who had multiorgan failure and were receiving mechanical ventilation to receive supplements of glutamine, antioxidants, both, or placebo. Supplements were started within 24 hours after admission to the ICU and were provided both intravenously and enterally. The primary outcome was 28-day mortality. Because of the interim-analysis plan, a P value of less than 0.044 at the final analysis was considered to indicate statistical significance.

RESULTS: There was a trend toward increased mortality at 28 days among patients who received glutamine as compared with those who did not receive glutamine (32.4% vs. 27.2%; adjusted odds ratio, 1.28; 95% confidence interval [CI], 1.00 to 1.64; P=0.05). In-hospital mortality and mortality at 6 months were significantly higher among those who received glutamine than among those who did not. Glutamine had no effect on rates of organ failure or infectious complications. Antioxidants had no effect on 28-day mortality (30.8%, vs. 28.8% with no antioxidants; adjusted odds ratio, 1.09; 95% CI, 0.86 to 1.40; P=0.48) or any other secondary end point. There were no differences among the groups with respect to serious adverse events (P=0.83).

CONCLUSIONS: Early provision of glutamine or antioxidants did not improve clinical outcomes, and glutamine was associated with an increase in mortality among critically ill patients with multiorgan failure. (Funded by the Canadian Institutes of Health Research; ClinicalTrials.gov number, NCT00133978.)

## Nutritional supplements

- As specific as possible to perceived nutritional deficiency
- Proteins
- Fatty acids
- Micronutrients
- Vitamins



### Proteins and amino acids

- All proteinogenic amino acids are important during wound healing
- Methionine, cysteine
- Arginine
- Supplementing with 9g of I-arginine has been shown to promote wound healing<sup>16</sup>
- An average dietary intake provides about 4g l-arginine per day<sup>30</sup>
- Arginine is conditionally essential, meaning that when we are healthy our bodies produce sufficient arginine however during healing requirements increases to a level where supplementation is recommended.



## Fatty acids

- Omega-3 fatty acids
- Essential polyunsaturated fatty acids
- Vital for normal metabolism but potential benefits of supplementation controversial



## Micronutrients

- Zinc
- Iron
- Selenium
- Copper
- Manganese



## Vitamins

• Vit C

- Vit A
- Vit B
- Vit E



### Arnica

A very popular supplement is **arnica montana**. Arnica is a mountain extract that has been used for many years.

It helps reduce and clear bruising and it also speeds the healing process after surgery. Available as a <u>cream</u> and in capsules. One of the most popular brands of capsules is <u>SinEcch</u>.



### Bromelain

Another well-known and popular substance is **Bromelain**. It is used to reduce bruising, swelling (edema), pain, and healing time. Certain claims are disputed because studies show mixed results.

Various studies however indicate that Bromelain reduces swelling, bruising, pain after surgery and physical injuries, and healing time. Bromelain is often used in conjunction with Quercetin. Quality brands that offer both in one are <u>NOW Foods</u> and <u>VitaMedica</u>.

#### Quercetin

**Quercetin**, a plant pigment naturally found in foods such as onions, is a so called bioflavonoid. It promotes histamine release in the body and thus acts like an anti-inflammatory. Usually after surgery inflammation is a common response by the body.

While it is totally normal, it can be quite uncomfortable and sometimes painful. Luckily Quercetin is known for its anti-inflammatory traits. On top of that, it is also know in speeding up the healing process. More about <u>bromelain and quercetin</u>.

### Probiotics

**Probiotics** are not only known for their specific healing benefits regarding certain surgeries but they are known to have beneficial effects in general.

Surgeryl patients often receive antibiotic treatment. This disrupts the gut flora and may create fungal disorders (including yeast infections), digestive problems, and diarrhea.

Probiotics can help neutralize these unwanted effects. After surgery, it's recommended to use a strain that contains acidophilus and bifida bacteria.

Enzymatic Therapy offers <u>Enzymatic Therapy Pearls Elite</u> and <u>Enzymatic Therapy – Pearls IC</u> which provide all strains known to improve our health. More about the <u>benefits of probiotics after surgery</u>.

### Aloe Vera and Centella Asiatica

Aloe Vera and Centella Asiatica, are botanicals that have been used for centuries to enhance wound healing. However, scientific research should be expanded to fully proof their efficacy.

In conclusion, all of these supplements have been found to be beneficial before, during, and after surgery. Many of these can be naturally found in your diet but intake by food is often not sufficient. Therefore, many medical professionals recommend to take supplements.

A popular, well-reviewed product containing all the essential nutrients is this **surgery healing supplements** and vitamins kit.

Why Take Supplements After Surgery?



## Hydration

- In long-term care, dehydration is one of the most common problems affecting good nutrition
- A general guide to providing fluids is 30-35mL/kg/day, with a minimum of 1500mL or 6-8 cups/day



### Nutritional intervention

Improve intake of food and fluids

- Improve nutritional quality of the food
- Remove barriers to food consumption
- Supplementation where requirements cannot be met by diet alone

### Factors that may hinder adequate nutrient intake

- Confusion and/or altered level of alertness
- Difficulty swallowing, e.g. due to Parkinson's disease or other neurological conditions
- Individual food preferences e.g. cultural food choices, vegetarian
- Lack of manual dexterity e.g. due to arthritis, peripheral vascular disease, neurological conditions
- Isolation, low socio-economic status
- Taste changes, reduced appetite, early satiety
- Feeding routines in institutions e.g. tray collection times.

- Poor eyesight
- Anxiety
- Poor dentition
- Pain
- Eating environment
- Packaging of food

### Ideas to improve nutritional status

- Offer food and fluids in a variety of textures and consistencies
- Offer assistance and allow sufficient time for meals and enlist family members or volunteers to help
- Provide encouragement, without pressuring
- Offer a variety of nutrient dense, high calorie and high protein meals
- Encourage grazing small frequent meals/snacks
- Encourage frequent drinking of fluids
- Provide hydration stations for patients to access drinks at any time
- Provide foods that patients like
- Position upright when eating
- Allow time for individuals to eat in a relaxed manner, with time to chew, feed themselves and finish their meal
- Provide a pleasant mealtime environment
- If the individual has dentures ensure that these are well fitted
- Explain that eating well, and eating the right foods, will aid recovery
- Provide assistance with the opening of containers, lids.

Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in nonmalnourished patients. van Anholt et al. Nutrition 2010; 26:867-72.

### N=43

A specific energy and protein enriched supplement, containing high levels of arginine, zinc, Vit C and antioxidants accelerated healing of pressure ulcers in non-malnourished patients in this DB-PRCT. Perioperative use of arginine-supplemented diets: A systematic review of the evidence. Drover et al. J Am Coll Surg 2011; 212:385-99. N = 35 RCTs, 3000 patients

750-1000ml for 5-7 days preop, then immediately postop via tube for 7 days, or until eating normally.

No difference in mortality

Reduction in infections by 41% (43% preop, 22% postop, 54% periop)

Reduction in LOS of median 2.38 days

IMPACT (omega-3 fatty acids, higher dose of arginine) appeared more beneficial

J Cancer Res Clin Oncol (2013) 139:1465–1470 DOI 10.1007/s00432-013-1466-5

ORIGINAL PAPER

### Randomized clinical trial of arginine-supplemented enteral nutrition versus standard enteral nutrition in patients undergoing gastric cancer surgery

Hongyan Zhao • Hongying Zhao • Yu Wang • Huang Jing • Qian Ding • Jun Xue

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#### Abstract

*Purpose* Significant malnutrition exists in a high percentage of patients with gastric cancer. It is, therefore, crucial to establish an effective means to provide nutrition for these patients. This prospective, randomized, doubleblinded clinical trial aims to assess the long-term survival of arginine-supplementation enteral nutrition versus standard enteral nutrition in malnourished patients with gastric cancer.

*Methods* The control group (36 cases) received postoperative standard enteral nutrition. Meanwhile, the argininesupplementation group (37 cases) adopted the same nutrition product but enriched with arginine (9.0 g/L). The primary study objective was overall survival (OS). Secondary endpoints were progression-free survival (PFS); serum parameters including total protein, albumin, proalbumin, and transferrin obtained on preoperative day 1, postoperative day 2, and day 12; CD4<sup>+</sup> and CD8<sup>+</sup> T cells, natural killer (NK) cells, immunoglobulin M (IgM), and immunoglobulin G (IgG) obtained on preoperative day 1 and postoperative day 7.

*Results* No significant differences in baseline characteristics were observed between groups. The group receiving arginine-enriched nutrition had a significantly better OS (P = 0.03, 41 vs. 30.5 months) and better PFS (P = 0.02, 18 vs. 11.5 months). On postoperative day 7, CD4<sup>+</sup> T cells, NK cells, IgM and IgG levels of the arginine-supplemented group increased prominently and were significantly higher than those of the control group and those on preoperative day 1. There is no significant difference in the serum total protein, albumin, proalbumin, and transferrin levels between the two arms.

*Conclusions* Arginine-supplemented enteral nutrition significantly improves long-term survival and restores immunity in malnourished gastric cancer.

Keywords Arginine · Malnutrition · Gastric cancer · Enteral nutrition



## Conclusion

- Local wound management, attenuating systemic inflammation and nutrition support are essential for optimal wound healing.
- Prompt assessment of nutritional status is necessary to start supplements early, if applicable.
- Immunonutrition seems to be especially beneficial.

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#### INTRODUCTION

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### WELCOME MESSAGE

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