
# REAL OR RUMOR IN CANCER NUTRITION



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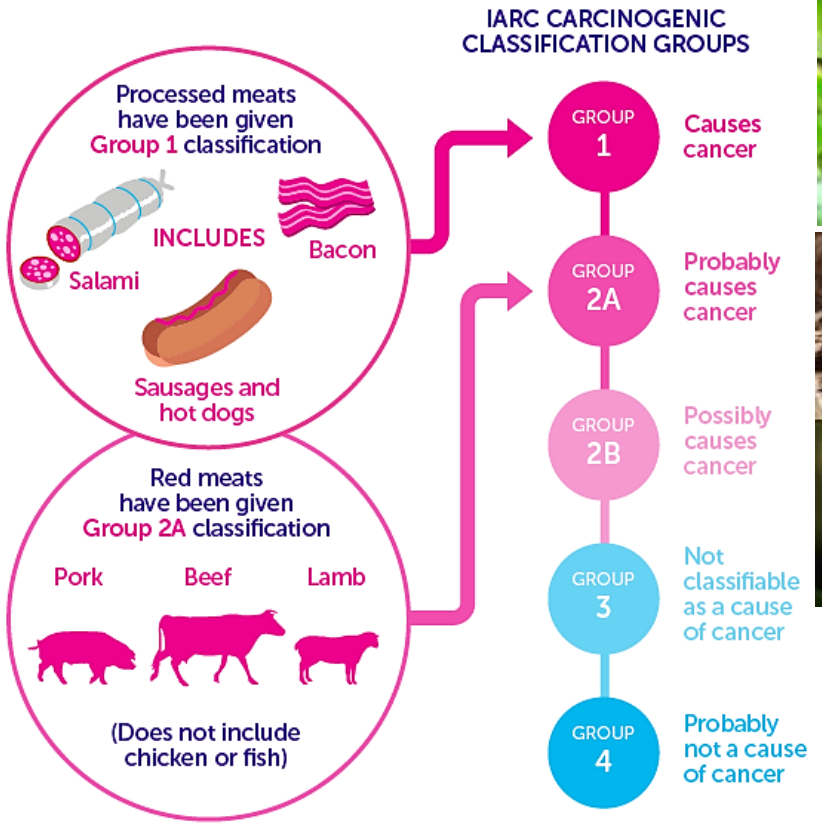
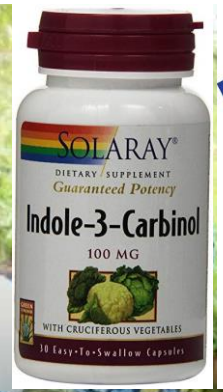
## MEAT AND CANCER
## HOW STRONG IS THE EVIDENCE?




These categories represent how likely something is to cause cancer in humans, not how many cancers it causes.

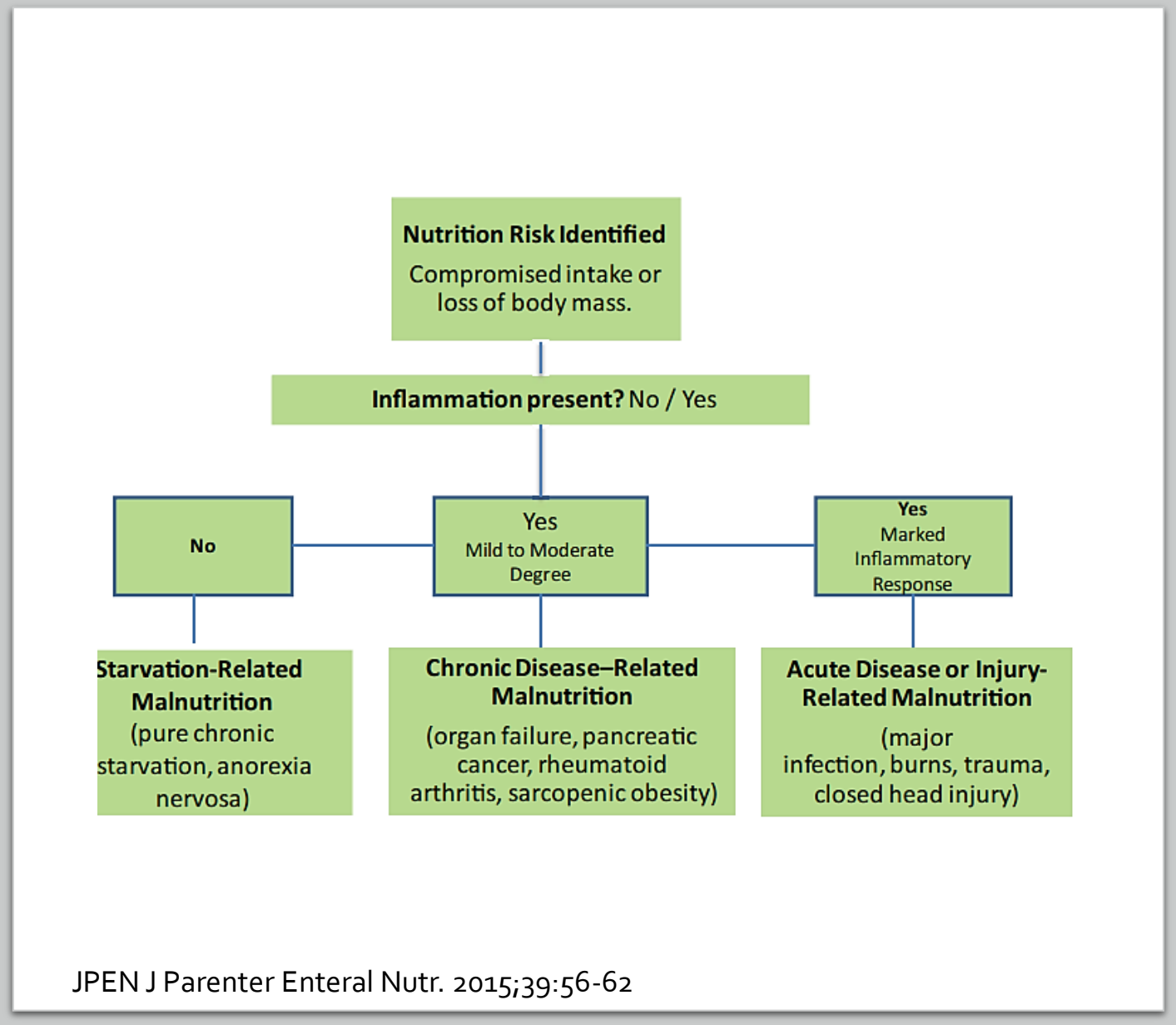






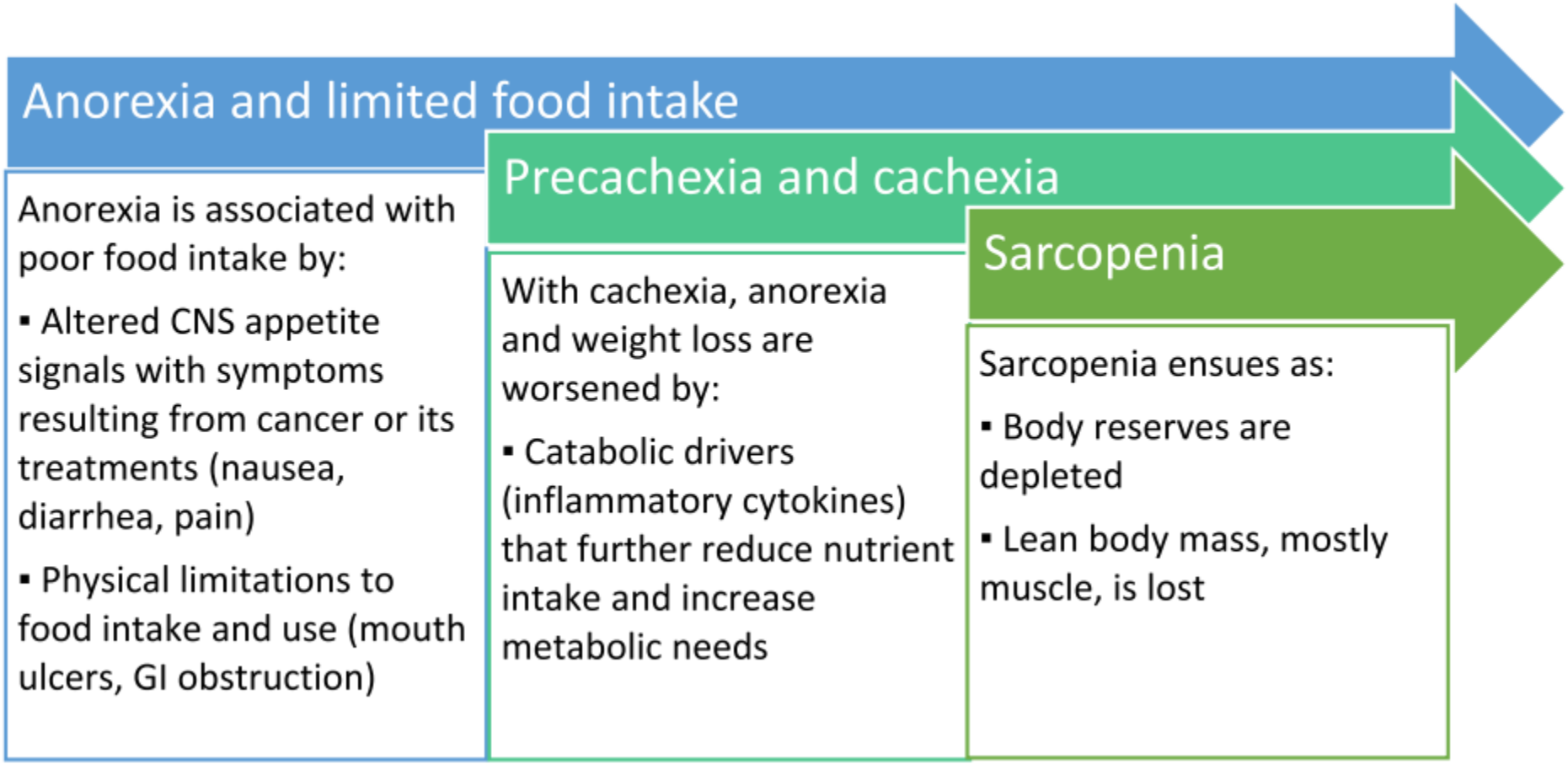

# Diagnosis of adult malnutrition syndromes. Etiology-based malnutrition definitions.

Adapted with permission from Jensen GL, Bistrian B, Roubenoff R, Heimburger DC. Malnutrition syndromes: a conundrum vs continuum. JPEN J Parenter Enteral Nutr. 2009;33:710-716.



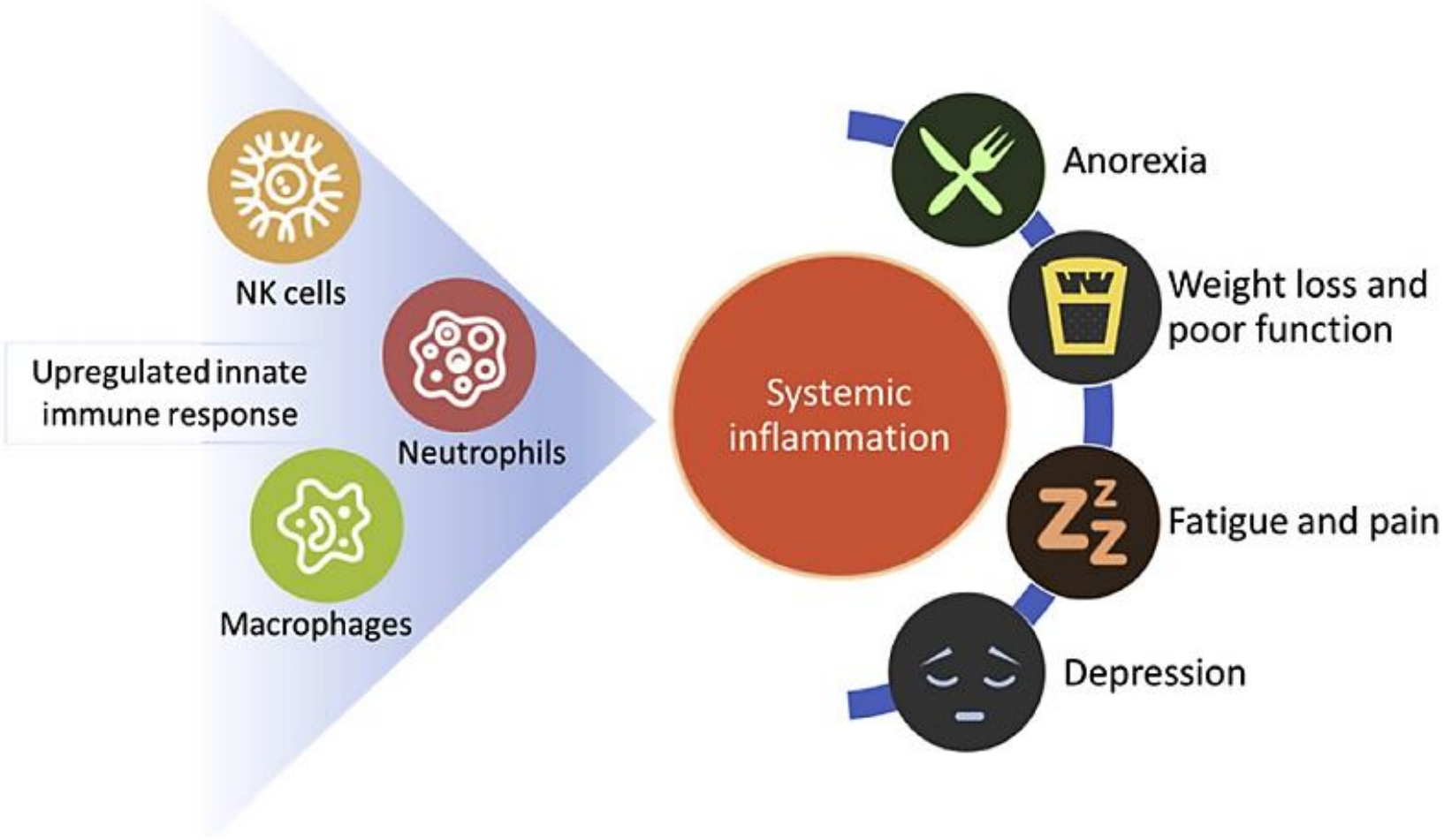

JPEN J Parenter Enteral Nutr. 2015;39:56-62

# Malnutrition in patients with cancer

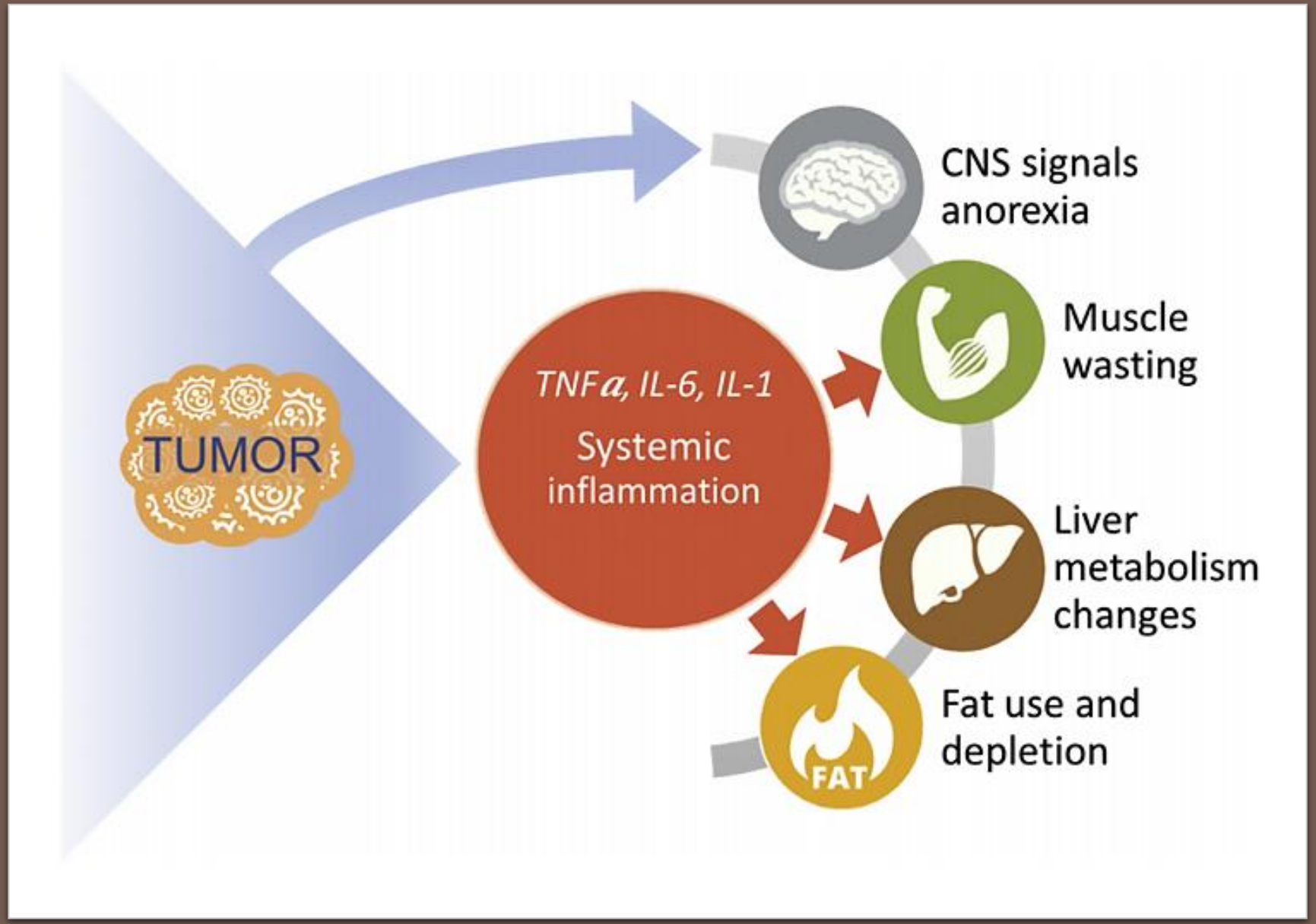



J. Arends et al. ESPEN expert group recommendations for action against cancer-related malnutrition. ***Clinical Nutrition***.2017;36:1187-1196.

Association of immunologic, metabolic, and clinical phenomena in cancer. In patients with cancer, systemic inflammation is associated with the host's innate immune response and with clinical symptoms.




Arends J. et al. ESPEN expert group recommendations for action against cancer-related malnutrition. ***Clinical Nutrition***.2017;36:1187-1196.




# Pathophysiology and metabolism in the presence of a tumor: the mechanisms.



Arends J. et al. ESPEN expert group recommendations for action against cancer-related malnutrition. ***Clinical Nutrition***.2017;36:1187-1196.


# Prevalence of Side Effects Affecting Nutrition

| Treatment | Weight loss | Fatigue | Nausea/vomiting | Oral mucositis | Taste alterations | Constipation |
|---|---|---|---|---|---|---|
| Overall % | 50%-90% | 70%-100% | 30%-90% | 40%-100% | 35%-70% | 40%-50% |
| Chemotherapy | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Radiation | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Surgery | ✓ | ✓ | ✓ | | | |
| Immunotherapy | ✓ | ✓ | | ✓ | | |

Information from Nutrition 411 (2012).
Check indicates Treatment in which side effects is common

Fearon K. C. H.. Cancer cachexia: Developing multimodal therapy for a multidimensional problem. ***European Journal of Cancer***. 2008;44(8), 1124–1132. doi:10.1016/j.ejca.2008.02.033

J Adv Pract Oncol. 2016 Apr; 7(3): 336–338.

# Prevalence and severity of weight loss in different primary cancers.

| | Primary % weight loss (median) | % of patients with ≥10% weight loss |
|---|---|---|
| Upper GI | 6.6 | 35 |
| Oesophagus | 15.1 | 66 |
| Stomach | 11.7 | 57 |
| Pancreas | 14 | 64 |
| Small bowel | 4.4 | 21 |
| Colon rectum | 4.8 | 28 |
| Lung | 6.4 | 35 |
| Upper respiratory | 5.4 | 25 |
| Others | 8.1 | 45 |

Bozzetti F. Nutritional Support in Patients with Cancer. In: Elia M, editors. ***Clinical Nutrition.*** 2nd ed. The Nutrition Society. Blackwell Publishing Ltd.;2013. P 385-419

Mariani, L., Lo Vullo, S., Bozzetti, F. et al. ***Support Care Cancer*** (2012) 20: 301. https://doi.org/10.1007/s00520-010-1075-7

# Health and financial impacts of malnutrition in patients with cancer reported in selected publications.

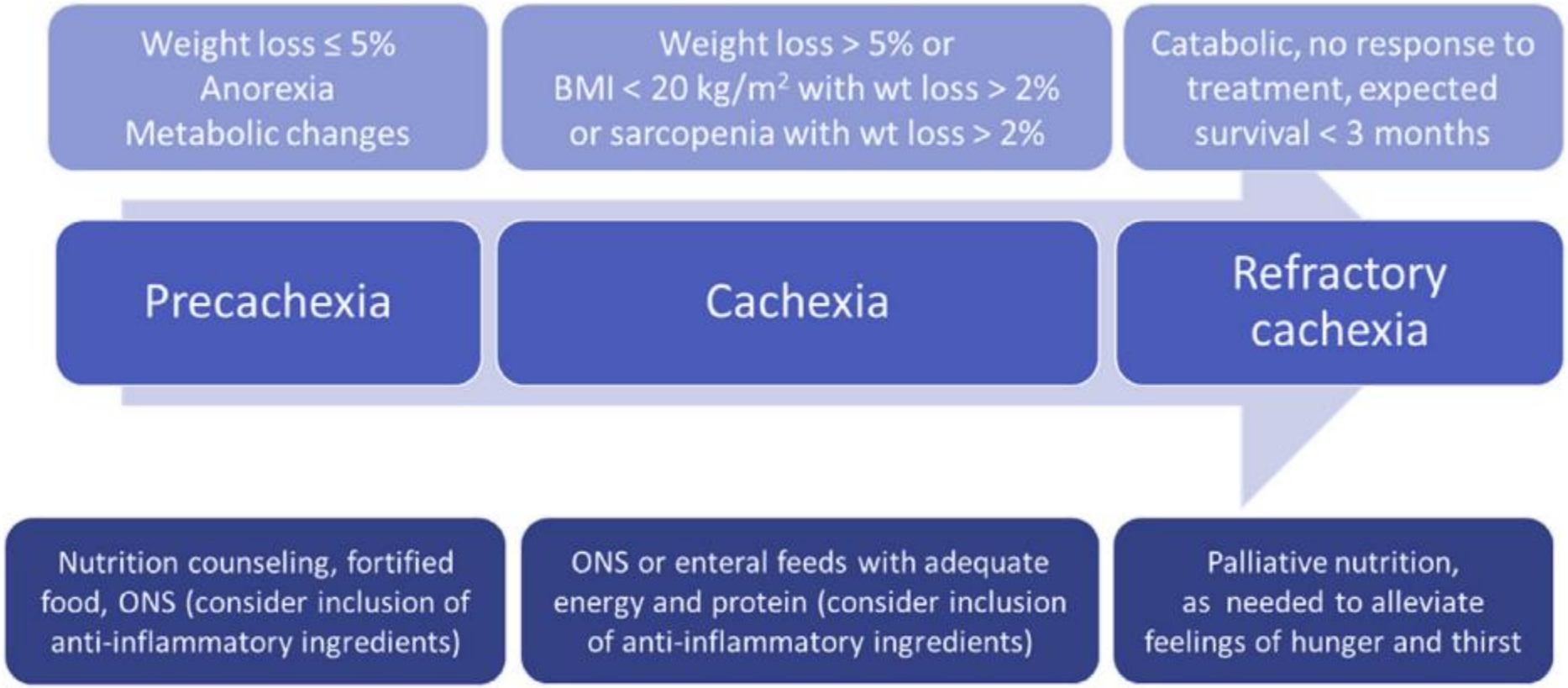
| Study, country | Cancer type | Negative impacts of malnutrition |
|---|---|---|
| Planas et al., 2016 [5] Spain | Multiple types | Significantly **longer LOS** (>3 days more) and **higher costs of care** (+€2000) for patients with malnutrition risk |
| Fukuda et al., 2015 [20] Japan | Gastric | Significantly **higher risk of surgical site infections** in malnourished compared to well-nourished patients (36% vs 14%, $P < 0.0001$) |
| Gellrich et al., 2015 [25] Switzerland | Oral | Malnourished patients had significantly **lower scores on QoL scales** related to physical function |
| Maasberg et al., 2015 [21] Germany | Neuroendocrine | Significantly **longer LOS** and **higher risk for mortality** in malnourished patients |
| Martin et al., 2015 [22] Canada | Multiple types | Weight-stable patients with BMI $\geq$25.0 kg/m$^2$ had the longest survival while **high % weight loss values associated with lowered categories of BMI were related to shortest survival** |
| Aaldriks et al., 2013 [19] Netherlands | Advanced colorectal | Malnutrition predicted **lower tolerance to chemotherapy** and was associated with greater **risk of mortality** |
| Freijer et al., 2013 [18] Netherlands | Multiple types | Disease-related malnutrition accounted for an excess €2 billion healthcare spending in a year; 1 of every €7 (about €300 million total) could be attributed to **excess healthcare spending on patients with cancer** |
| Pressoir et al., 2010 [1] France | Multiple types | Compared with adequately nourished patients, malnourished patients required **more antibiotic treatments** (36% vs 23%, $P < 0.0001$) and had significantly **longer LOS**<br>Severely malnourished patients were at **4-fold higher risk of 2-month mortality** than well-nourished patients |

Abbreviations: length of stay, LOS; body mass index, BMI; quality of life, QoL.

Arends J. et al. ESPEN expert group recommendations for action against cancer-related malnutrition. ***Clinical Nutrition***.2017;36:1187-1196.

# Medical nutrition care depends on a patient's nutritional and metabolic needs, which are related to cancer stage and nutritional status.



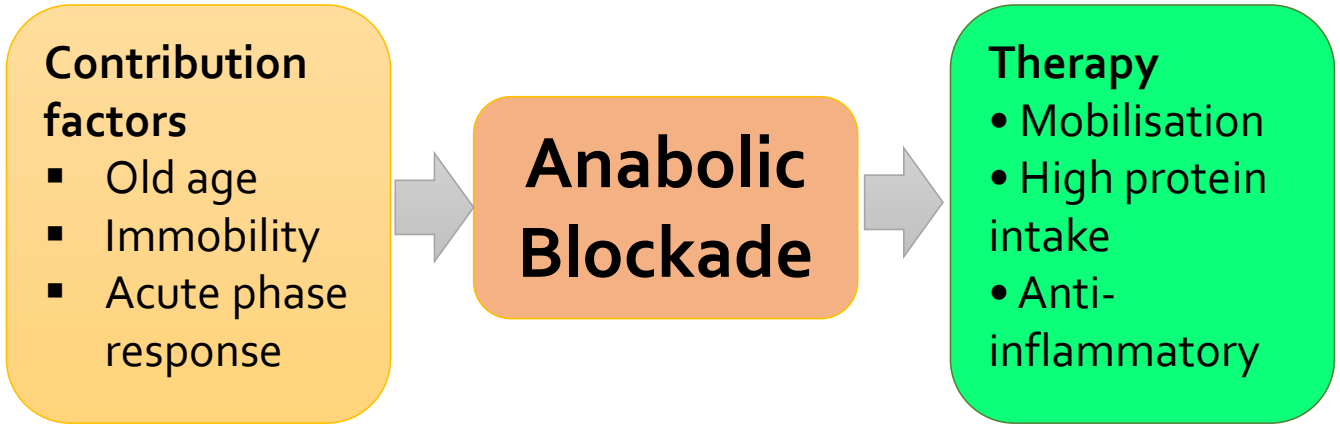


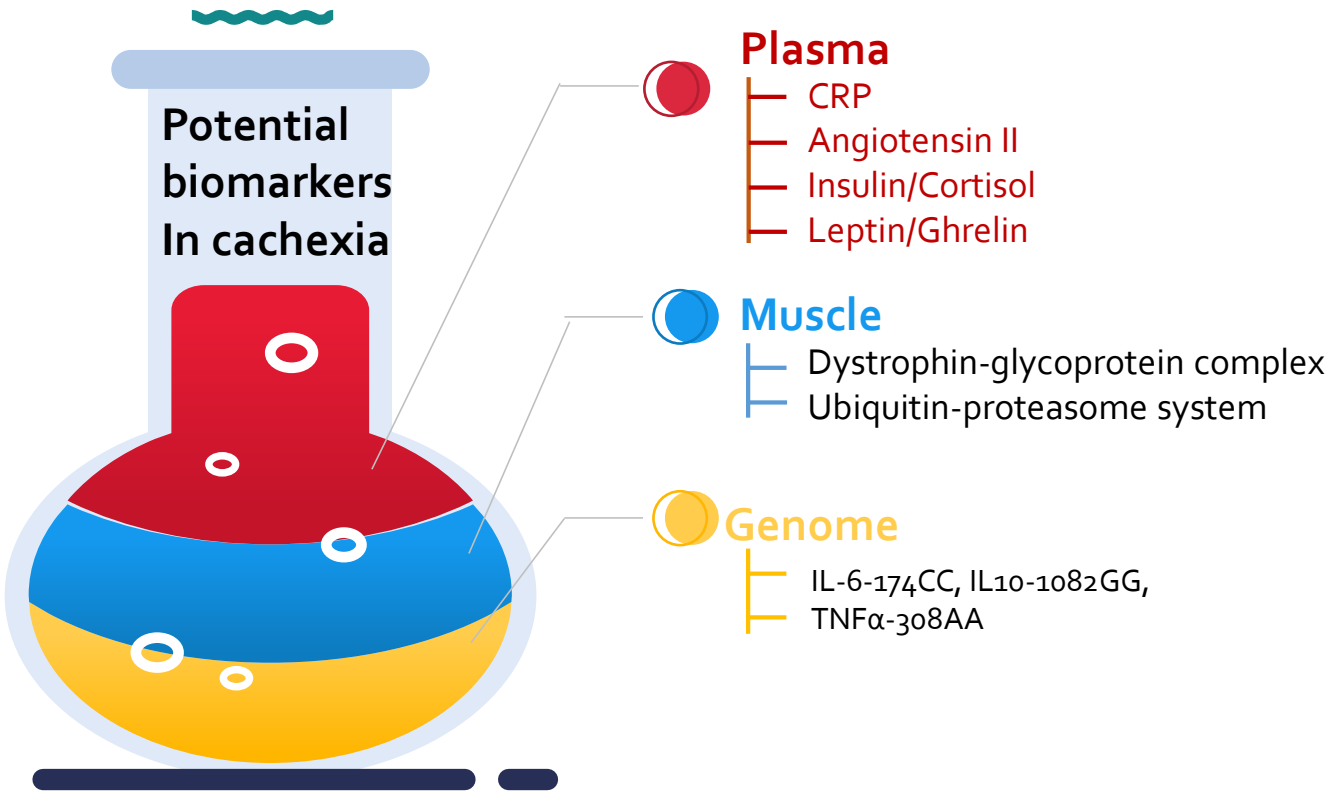

J. Arends et al. ESPEN expert group recommendations for action against cancer-related malnutrition. ***Clinical Nutrition***.2017;36:1187-1196.

# Scope

- **Dietary Counseling**
  - Oral Intake
  - Food modified
  - Oral Nutrition Support

Nutrition Support
- EN, Tube feeding
- PN, Parenteral Nutrition




Fearon K.C.H. Cancer cachexia: Developing multimodal therapy for a multidimensional problem. ***European Jounal Of Cancer***. 2008;44:1124–1132.


# Nutrition Support Guideline Recommendations During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation



| Guideline Recommendation | Grade |
|---|---|
| **A. Nutrition Support Therapy During Anticancer Treatment** | |
| 1. Patients with cancer are nutritionally-at-risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. | D |
| 2. Nutrition support therapy ***should not be used routinely*** in patients undergoing major cancer operations. | A |
| 3. Perioperative nutrition support therapy may be beneficial in moderately or severely malnourished patients if administered for 7-14 days preoperatively, but the potential benefits of nutrition support must be weighed against the potential risks of the nutrition support therapy itself and of delaying the operation. | A |
| 4. Nutrition support therapy ***should not be used routinely*** as an adjunct to chemotherapy. | B |
| 5. Nutrition support ***therapy should not be used routinely*** in patients undergoing head and neck, abdominal, or pelvic irradiation. | B |
| 6. Nutrition support therapy is appropriate in patients receiving active anticancer treatment who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time (see Guideline 6 Rationale for discussion of "prolonged period of time"). | B |
| 7. The palliative use of nutrition support therapy in terminally ill cancer patients is rarely indicated. | B |
| 8. **ω-3 Fatty acid supplementation** may help stabilize weight in cancer patients on oral diets experiencing progressive, unintentional weight loss. | B |
| 9. Patients should not use therapeutic diets to treat cancer. | E |
| 10. Immune-enhancing enteral formulas containing mixtures ***of arginine, nucleic acids, and essential fatty acids may be beneficial*** in malnourished patients undergoing major cancer operations. | A |


# Nutrition Support Guideline Recommendations During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation



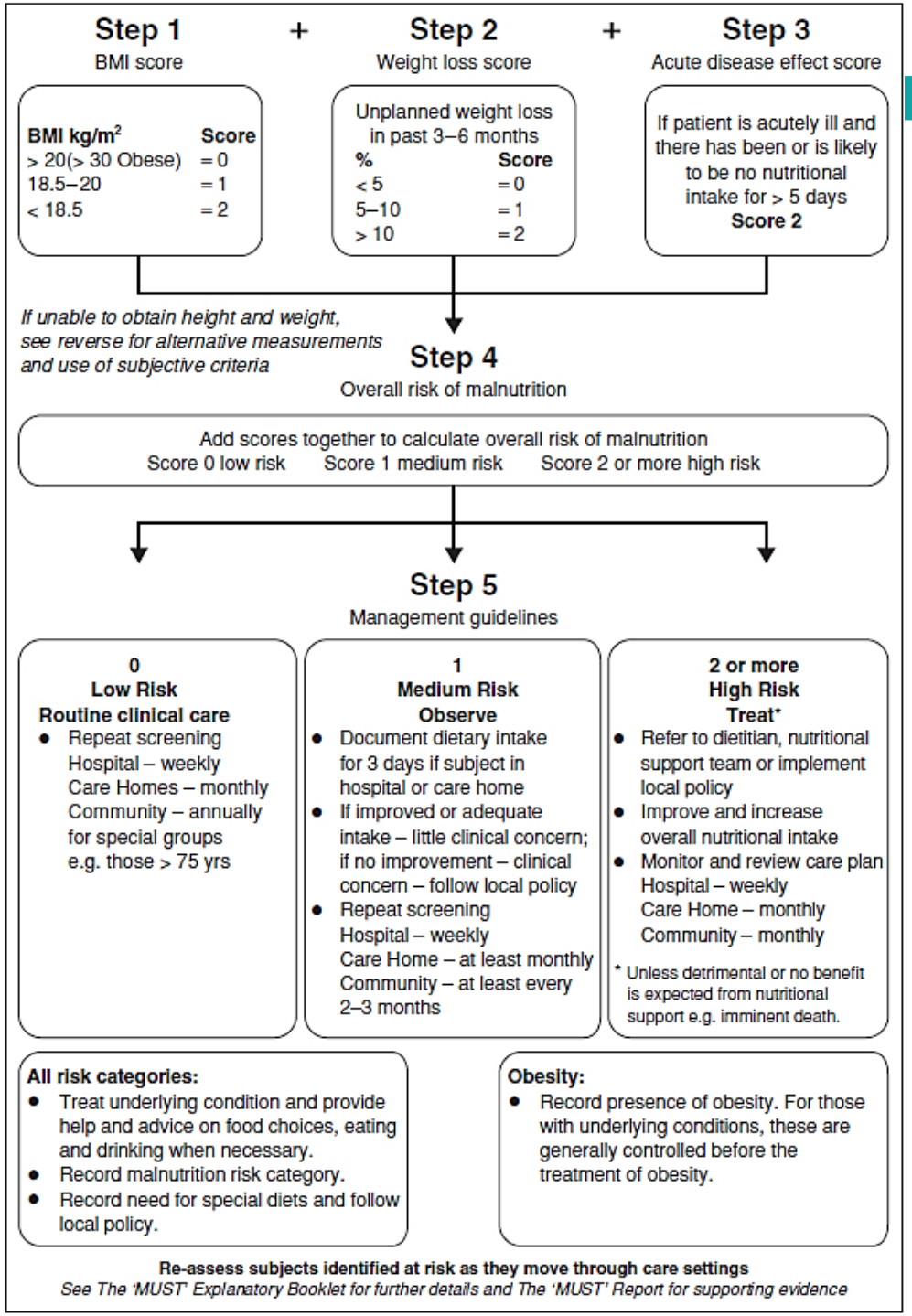
| Guideline Recommendation | Grade |
|---|---|
| **B. Nutrition Support Therapy in Hematopoietic Cell Transplantation** | |
| 1. All patients undergoing hematopoietic cell transplantation with myeloablative conditioning regimens are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. | D |
| 2. Nutrition support therapy is appropriate in patients undergoing hematopoietic cell transplantation who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time (see Guideline 6 Rationale for discussion of "prolonged period of time").When parenteral nutrition is used, it should be discontinued as soon as toxicities have resolved after stem cell engraftment. | B |
| 3. Enteral nutrition should be used in patients with a functioning gastrointestinal tract in whom oral intake is inadequate to meet nutrition requirements | C |
| 4. Pharmacologic doses of parenteral glutamine may benefit patients undergoing hematopoietic cell transplantation.* | C |
| 5. Patients should receive dietary counseling regarding foods which may pose infectious risks and safe food handling during the period of neutropenia. | C |
| 6. Nutrition support therapy is appropriate for patients undergoing hematopoietic cell transplantation who develop moderate to severe graft-vs-host disease accompanied by poor oral intake and/or significant malabsorption. | C |



August DA et al. A.S.P.E.N. Clinical Guidelines: Nutrition Support Therapy During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation. ***J Parenter Enteral Nutr.*** 2009;33:472-500.

# Malnutrition Universal Screening Tool (MUST) for adults

Chemotherapy agents associated with taste and smell alterations include **carboplatin, cisplatin, cyclophosphamide, docetaxel, doxorubicin, fluorouracil, methotrexate, paclitaxel, and tegafur**






http://lllnutrition.com/mod_lll/TOPIC3/m31.htm

# Hospital: Nutritional Risk Screening (NRS)

**Nutritional Risk Screening (NRS 2002); Initial screening questions**

| **Initial screening I** | | Yes | No |
|---|---|---|---|
| 1 | Is BMI < 20.5? | | |
| 2 | Has the patient lost weight within the last 3 months? | | |
| 3 | Has the patient had a reduced dietary intake in the last week? | | |
| 4 | Is the patient severely ill? (e.g. in intensive therapy) | | |

**Yes:** If the answer is 'Yes' to any question, the final screening is performed.
**No:** If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient is (e.g.) scheduled for a major operation, a preventative nutritional care plan is considered to try to avoid the associated risk.

***Aims of nutrition therapy***

- To maintain or improve food intake and mitigate metabolic derangements
- Maintain skeletal muscle mass and physical performance, reduce the risk of reductions or interruptions of scheduled anticancer treatments
- Improve quality of life.

**Nutritional Risk Screening (NRS 2002); Final screening**

| **Final screening II** | | | |
|---|---|---|---|
| **Impaired nutritional status** | | **Severity of disease** (≈ increase in requirements) | |
| Absent **Score 0** | Normal nutritional status | Absent **Score 0** | Normal nutritional requirements |
| Mild **Score 1** | Wt loss >5% in 3 months<br>or<br>Food intake below 50-75% of normal requirement in preceding week | Mild **Score 1** | Hip fracture<br>Chronic patients, in particular with acute complications: cirrhosis, COPD<br>Chronic hemodialysis, diabetes, oncology |
| Moderate **Score 2** | Wt loss >5% in 2 months<br>or<br>BMI 18.5 - 20.5 + impaired general condition<br>or<br>Food intake 25-50% of normal requirement in preceding week | Moderate **Score 2** | Major abdominal surgery<br>Stroke<br>Severe pneumonia, hematologic malignancy |
| Severe **Score 3** | Wt loss >5% in 1 months (>15% in 3 months)<br>or<br>BMI < 18.5 + impaired general condition<br>or<br>Food intake 0-25% of normal requirement in preceding week | Severe **Score 3** | Head injury<br>Bone marrow transplantation<br>Intensive care patients (APACHE>10) |
| **Score:** + | | **Score:** | **=Total score:** |
| **Age** | if ≥ 70 years: add 1 to total score above | | **= age-adjusted total score:** |
| **Score ≥ 3: the patient is nutritionally at-risk and a nutritional care plan is initiated.**<br>**Score < 3: weekly re-screening of the patient. If the patient is (e.g.) scheduled for a major operation, a preventative nutritional care plan is considered to try to avoid the associated risk.** | | | |



http://lllnutrition.com/mod_lll/TOPIC3/m31.htm

| **Nutrition Assessment form** : | | | Moderate malnutrition risk | | | | HN | 8001xxxxxx2 |
|---|---|---|---|---|---|---|---|---|
| **Height** | 152 | **cm** | **BMI** | 33.72 | **Kg/m²** | | | 20-Aug-19 15 |
| **Weight** | 77.9 | **Kg** | **IBW** | 46.8 | **Kg** | **Basal Energy Expenditure (BEE)** | 1079.1 | **kcal/day** |
| **Age** | 79 | **yr** | **%IBW** | 166 | | **Total Energy Expenditure (TEE)** | 1511 | **kcal/day** |
| **Activity factor** | 1.4 | | **Adj BW** | 54.6 | **Kg** | | 27.68 | **kcal/kg/day** |
| **Protein factor** | 1.2 | **g/kg/day** | | | | Protein Need | 93.48 | **g/day** |
| **Sex** | Female | | | | | | | |
| **Usual BW** | N/A | Kg | | | Food Allergy | NKA | | |
| Diet Prior to admission | | | Normal | | Admission date | 16-Aug-19 | | |
| Diagnosis | right breast mass PMH:HTN, CKD stage III, and hypercalcemia | | | | | | | |
| Patient related medical history | | | | | | | | |

| Nutritional Parameters | A ( Score = 1) | | B ( Score = 2) | | C ( Score = 3) | |
|---|---|---|---|---|---|---|
| **BMI (kg/m²)** | | 18.50 - 24.99 | ✓ | 25-39.99 or 16-18.49 | | ≥ 40 or < 16 |
| **Weight loss (past 3 – 6 mo.)** | ✓ | < 5% usual BW or N/A | | 5-10% usual BW | | >10% usual BW |
| **Currently Dietary intake (≥4 days)** | ✓ | Adequate (>75% of TEE) | | Inadequate – hypocaloric (50-75% of TEE) | | Inadequate – starvation (NPO< 50% of TEE) |
| **Current intake vs usual** | ✓ | Increase/no change | | Slightly decrease | | Severe decrease |
| **Gastrointestinal symptoms** | | No symptoms | ✓ | One or more symptoms ; not daily | | Some or all symptoms ; Daily |
| **Duration of gastrointestinal symptoms** | ✓ | N/A or < 1 week | | 1-2 weeks | | ≥ 2 weeks |
| **Functional capacity** | ✓ | No dysfunction | | Difficulty with ambulation | | Bed/chair-ridden |
| **Serum albumin level** | ✓ | N/A | | 2.5 - 3.5 gm/d | | < 2.5 gm/d |
| | 6 | | 4 | | 0 | |
| Total score | 10 | Moderate risk | >15 points = High risk; 10-14 points = Moderate risk; <10 point = Low risk | | | |

# Specific chemotherapy-induced micronutrient imbalance

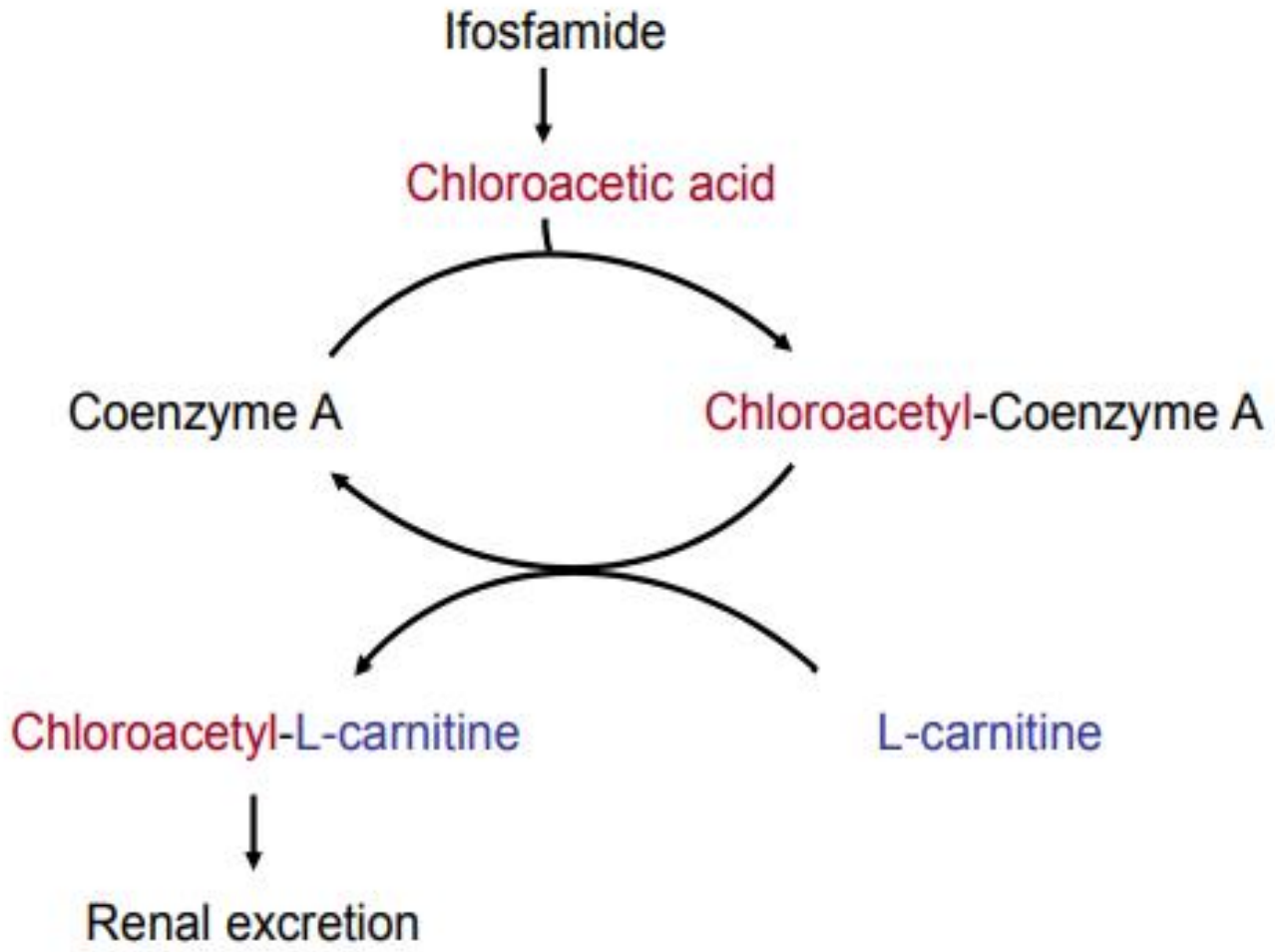


| Cytostatic Agent | Micronutrient | Mechanism | Possible Consequences |
|---|---|---|---|
| Cisplatin | L-carnitine | Increased renal excretion of L-carnitine | Cisplatin-induced carnitine insufficiency, increased risk of complications (e.g., fatigue) |
| Cisplatin | Magnesium, Potassium | Increased renal excretion of Magnesium and Potassium | Hypomagnesemia, Hypokalemia, Disorders of lipid metabolism, Glucose intolerance, Increased nephrotoxicity |
| Cyclophosphamide | Vitamin D | Increased breakdown of Calcidiol and Calcitriol to inactive metabolites by 24-hydroxylase | Vitamin D deficiency (Calcidiol <20 ng/mL), Risk of metabolic bone disorders and Impaired immunocompetence |
| Fluorouracil | Vitamin B1 | Inhibition of phosphorylation of Thiamine to active coenzyme Thiamine Diphosphate | Risk of cardiac failure, Lactic acidosis, Neurotoxicity |
| Ifosfamide | L-carnitine | Increased renal excretion of L-carnitine | Ifosfamide-induced Carnitine Insufficiency, Increased risk of complications (e.g., fatigue) |
| Methotrexate | Folic acid | Folic acid antagonism | Folate deficiency, Homocysteinemia, Mucositis |
| Paclitaxel | Vitamin D | Increased breakdown of Calcidiol and Calcitriol to inactive metabolites by 24-hydroxylase | Vitamin D deficiency (Calcidiol <20 ng/mL), Risk of metabolic bone disorders and Impaired immunocompetence |
| Pemetrexed | Folic acid | Folic acid antagonism | Mucositis, Diarrhea, Thrombocytopenia, Neutropenia, Homocysteinemia |



***Nutrients*** 2016, 8, 163; doi:10.3390/nu8030163

# Ifosfamide and carnitine depletion

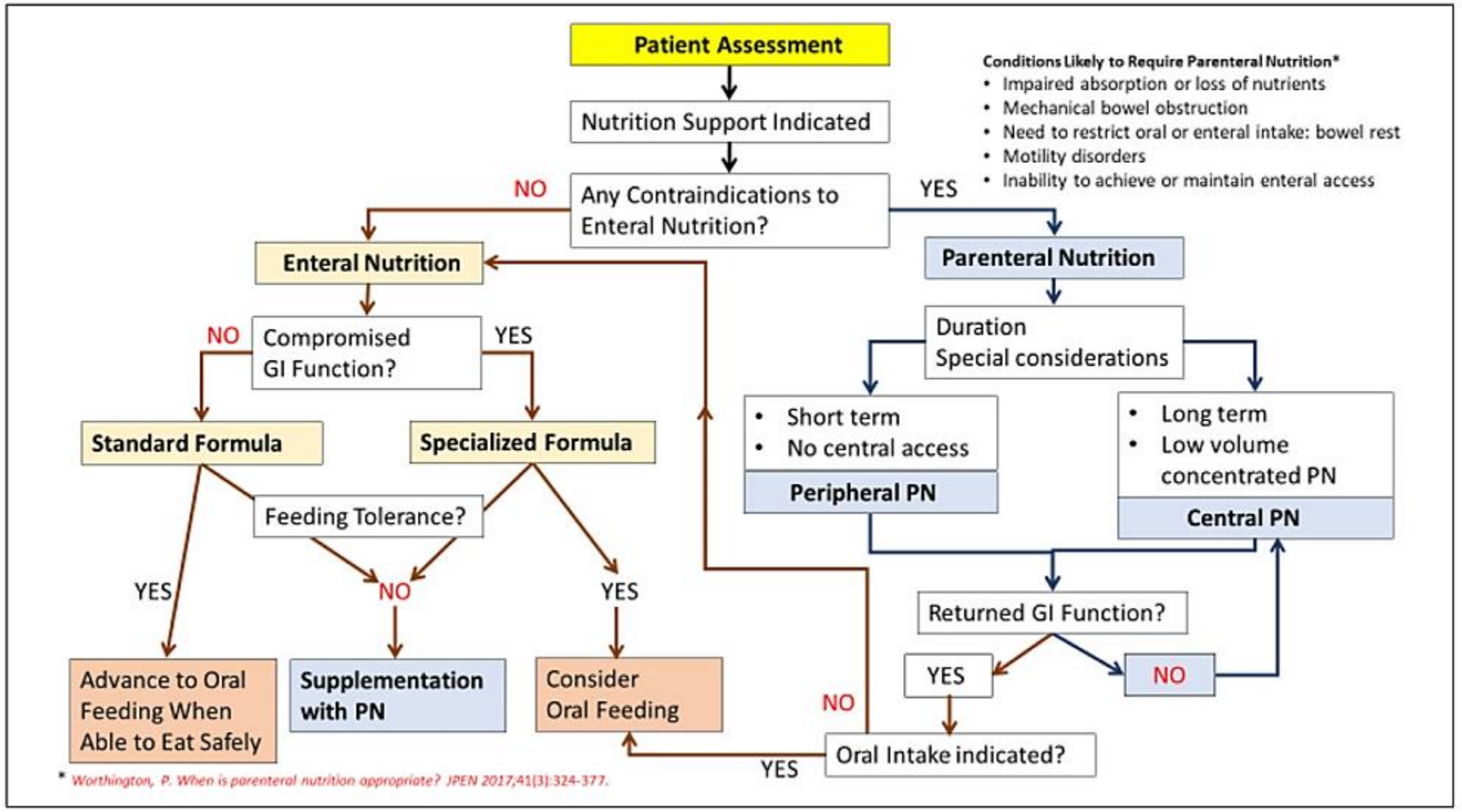





***Nutrients*** 2016, 8, 163; doi:10.3390/nu8030163

# Standards for Nutrition Support: Adult Hospitalized Patients






***Nutr Clin Pract***. 2018;33:906–920


# ESPEN 2016

Therapies for cancer-associated malnutrition

1. Nutrition Counseling by a healthcare professional is regarded as the 1st line of nutrition therapy
   - Counseling to help manage symptoms and encourage the intake of energy-enriched foods and fluids → lead to lasting change in eating habits
     - A diet enriched in energy and protein is preferred
     - The best way to maintain or increase energy and protein intake is with normal food but often difficult
2. Artificial nutrition are most often recommended to supplement volitional food intake
   - If patients are unable to eat adequately (e.g. no food for more than one week or less than 60% of requirement for more than 1-2 weeks)
   - Supplemental or complete nutrition by the oral, enteral or parenteral route may be indicated, depending on the level of function of the GI tract
3. Theoretical arguments that nutrients "feed the tumor" are ***not supported by evidence related to clinical outcome*** and should not be used to refuse, diminish, or stop feeding

# Nutrition Support: Suggested Nutrient Intake for Adult Cancer Patient

| | Stable Patients and Outpatient | Critically ill Cancer Patients |
|---|---|---|
| Total Calories | 30*-35 kCal/kg/d<br>* Esophagus, Gastric, Colorectal CA | 25-30 kCal/kg/d<br>GVHD 30-50 kCal/kg/day |
| Protein | > 1.4 Gm/kg/d | 1.2-1.5 Gm/kg/d<br>GVHD 1.5-2 Gm/kg/d |
| Fat | 1-2 gm/kg/day | |
| Protein: Fat: Carbohydrate | 15%: 30%: 55% (≤ 5-7 mg/kg/min) | 15%: 30%: 55% (≤ 4 mg/kg/min) |
| Fluid | 30-40 mL/kg | Minimum needed to deliver adequate macronutrient |
| Calcium | 10-15 mEq/Day | |
| Magnesium | 8-20 mEq/Day | |
| Phosphorus | 20-40 mMol/Day | |
| Sodium | 1-2 mEq/kg/Day | |
| Potassium | 1-2 mEq/kg/Day | |
| Acetate | As needed | |
| Chloride | As needed | |

Arends J, et al., ESPEN guidelines on nutrition in cancer patients, Clinical Nutrition (2016), http://dx.doi.org/10.1016/j.clnu.2016.07.015
Lach K. and Peterson SJ. Nutrition Support for Critically Ill Patients With Cancer. ***Nutr Clin Pract.*** 2017;32:578-586.
Ceolin Alves et al. Energy Expenditure in Patients With Esophageal, Gastric, and Colorectal Cancer. ***J Parenter Enteral Nutr.*** 2016;40:499-506

# Laboratory monitoring of hospitalized adult patients on parenteral nutrition



**TABLE 14-5 Suggested Monitoring for Parenteral Nutrition[6,44]**

| Parameter | Baseline | Initiation | Critically Ill Patients | Stable Patients |
|---|---|---|---|---|
| CBC with differential | Yes | | Weekly | Weekly |
| INR, PT, PTT | Yes | | Weekly | Weekly |
| Electrolytes: Na, K, Cl, $CO_2$ Mg, Ca, phosphorus, BUN, Cr | Yes | Daily × 3 | Daily | 1–2 × per week |
| Serum triglycerides | Yes | Day 1 | Weekly | Weekly |
| Transferrin or prealbumin | Yes | | Weekly | Weekly |
| Serum glucose | Yes | Daily × 3 | Daily | 1–2 × per week |
| Capillary glucose | | As needed | At least 3 × day until consistent less than 150 mg/dL | As needed |
| Weight | Yes | Daily | Daily | 2–3 × per week |
| Intake and output | Yes | Daily | Daily | Daily unless fluid status assessed by physical exam |
| ALT, AST, ALP, total bilirubin | Yes | Day 1 | Weekly | Monthly |
| Nitrogen balance | As needed | | As needed | As needed |

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CBC, complete blood cell count; Cl, chloride; $CO_2$, bicarbonate; Cr, serum creatinine; INR, International Normalized Ratio; K, potassium; Na, sodium; PT, prothrombin time; PTT, partial thromboplastin time.

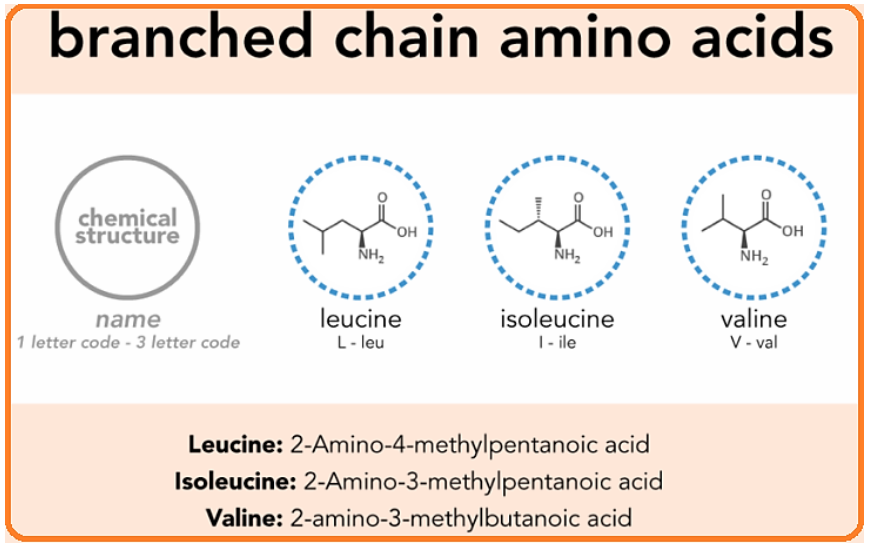
# ESPEN 2016

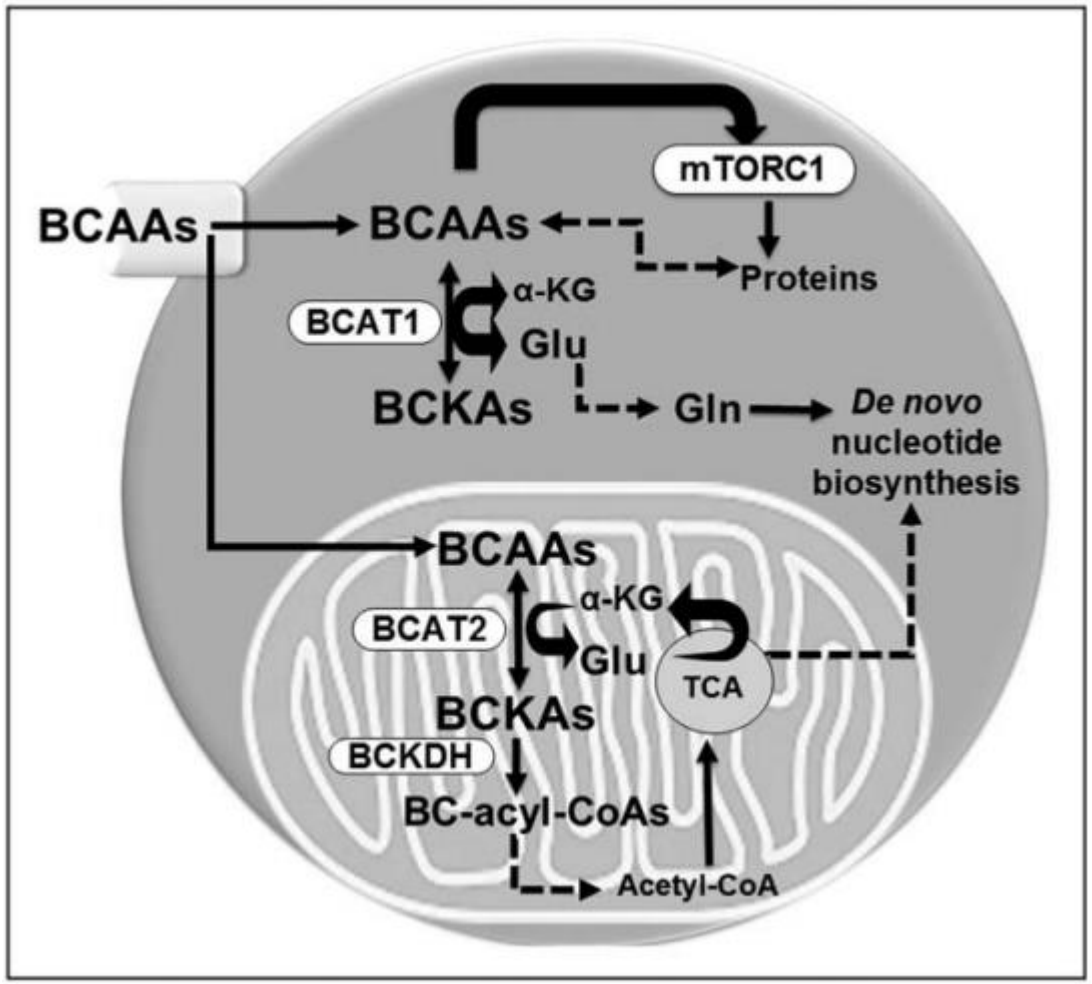
## Refeeding Syndrome Prevention

- Risk of developing refeeding syndrome increases with the degree of the patient's nutritional depletion.
- In patients with minimal food intake for at least 5 days, it has been recommended that no more than half of the calculated energy requirements be supplied during the first 2 days of feeding.
- If depletion is severe, initial ***energy supply should not exceed 5-10 kcal/kg/day and then a slow increase of energy intake over 4-7 days*** can be provided until full substitution of requirements is reached.
- Volume of circulation, fluid balance, heart rate and rhythm, as well as clinical status should be monitored closely.
- Before and during nutritional repletion it is prudent to supply ***vitamin B1 in daily doses of 200-300 mg*** as well as a balanced micronutrient mixture.
- The following electrolytes should be monitored and substituted, if necessary, by the oral, enteral, or parenteral route:
  - Potassium (requirement approximately 2-4 mmol/kg/day),
  - Phosphate (requirement approximately 0.3-0.6 mmol/kg/day)
  - Magnesium (requirement approximately 0.2 mmol/kg/day if supplied intravenously or 0.4 mmol/kg/day if supplied orally)

# 2016 ESPEN guidelines on nutrition in cancer patients

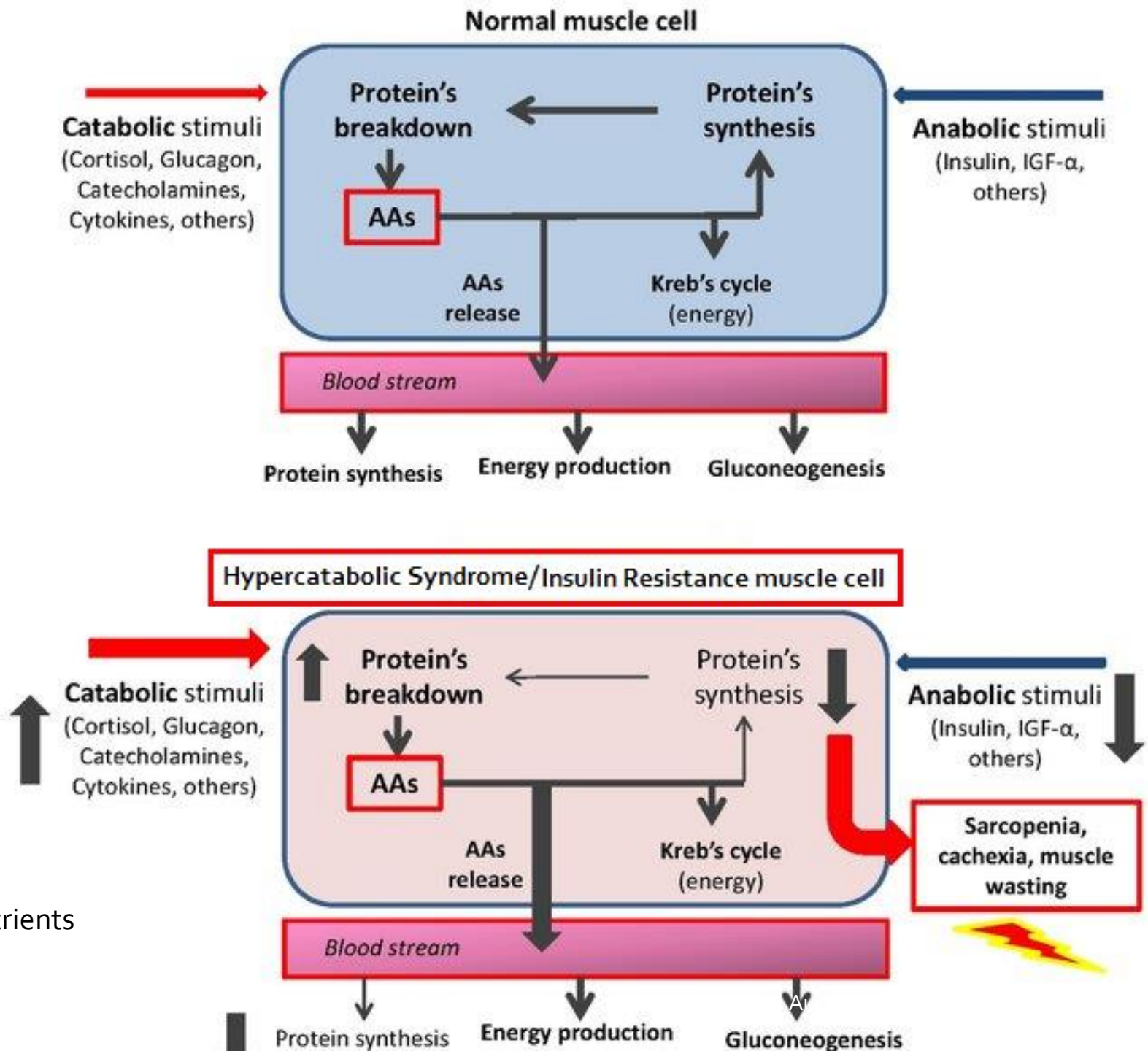
- Total parenteral nutrition enriched with branched chain amino acids (BCAA) resulted in an ***improved protein accretion and albumin synthesis*** when compared to standard amino acid solutions.
- Deutz et al. reported the findings of a randomized clinical trial, showing that the administration of ***40 g of amino acids (0.48 g/kg) when given as an oral nutritional supplement enriched in leucine and N-3 fatty acids*** to non-malnourished patients with advanced cancer, led to a significant increase in the fractional synthetic rate of muscle protein when compared to feeding a conventional supplement containing 24 g of protein.




Curr Opin Clin Nutr Metab Care 2018, 21:64–70
DOI:10.1097/MCO.0000000000000430

# The fate of amino acids (AAs) in muscle cell:




***Nutrients*** 2018,10, 391;
doi:10.3390/nu10040391www.mdpi.com/journal/nutrients

# Foods High in BCAAs

| Food | Serving | Protein | BCAAs | Leucine | Isoleucine | Valine | BCAA (per g of protein | Leucine (per g of protein) |
|---|---|---|---|---|---|---|---|---|
| Chicken Breast | 6 Oz | 36 g | 6.6 g | 2.9 g | 1.8 g | 1.9 g | 0.18 | 0.08 |
| 95% lean beef | 6 Oz | 36 g | 6.2 g | 2.8 g | 1.6 g | 1.8 g | 0.17 | 0.08 |
| Canned Tuna | 6 Oz | 33 g | 5.6 g | 2.5 g | 1.5 g | 1.6 g | 0.17 | 0.08 |
| Wild Salmon | 6 Oz | 34 g | 5.9 g | 2.7 g | 1.5 g | 1.7 g | 0.17 | 0.08 |
| Beef Flank Steak | 6 Oz | 36 g | 6.2 g | 2.8 g | 1.6 g | 1.8 g | 0.17 | 0.08 |
| Talapia | 6 Oz | 34 g | 5.9 g | 2.7 g | 1.6 g | 1.6 g | 0.17 | 0.08 |
| Turkey Breast | 6 Oz | 40 g | 5.2 g | 2.8 g | 1.1 g | 1.3 g | 0.13 | 0.07 |
| Egg | 1 | 6.3 g | 1.3 g | 0.54 g | 0.3 g | 0.4 g | 0.21 | 0.09 |
| Egg White | 1 | 3.6 g | 0.8 g | 0.3 g | 0.2 g | 0.3 g | 0.23 | 0.09 |
| Roasted Peanuts | 6 Oz | 12 g | 6.8 g | 3.1 g | 1.7 g | 2 g | 0.14 | 0.07 |


| สารอาหาร | ต่อ 100 กิโลแคลอรี่ | ต่อปริมาตร 200 มล. | ปริมาณสารอาหารใน 200 มล.เปรียบเทียบเป็น% กับ WHO RNI* |
|---|---|---|---|
| Energy, KCal | 100 | 210 | ** |
| Protein, gm | 6.4 | 13.5 | 27 |
| Carbohydrate, gm | 15.4 | 32.4 | ** |
| Fat, gm | 1.7 | 3.5 | ** |
| Amino Acids | | | |
| Valine, gm | 0.78 | 1.635 | 104.8 |
| Leucine, gm | 0.97 | 2.03 | 86.8 |
| Isoleucine, gm | 0.84 | 1.76 | 146.7 |
| Threonine, gm | 0.14 | 0.29 | 32.2 |
| Tryptophan, gm | 0.04 | 0.08 | 33.3 |
| Methionine, gm | 0.03 | 0.06 | 10.0 |
| Phenylalanine, gm | 0.08 | 0.16 | ** |
| Alanine, gm | 0.31 | 0.655 | ** |
| Arginine, gm | 0.33 | 0.695 | ** |
| Histidine, gm | 0.11 | 0.235 | 39.2 |
| Proline, gm | 0.47 | 0.98 | ** |
| Serine, gm | 0.10 | 0.215 | ** |

| Each 1000 mL contains: | |
|---|---|
| L-Threonine | 4.5 g |
| L-Serine | 5 g |
| L-Proline | 8 g |
| L-Cysteine HCl monohydrate | 0.4 g |
| (L-Cysteine equivalent) | 0.3 g |
| Aminoacetic acid | 9 g |
| L-Alanine | 7.5 g |
| L-Valine | 8.4 g |
| L-Methionine | 1 g |
| L-Isoleucine | 9 g |
| L-Leucine | 11 g |
| L-Phenylalanine | 1 g |
| L-Tryptophan | 0.7 g |
| Lysine HCl | 7.6 g |
| (L-Lysine equivalent) | 6.1 g |
| L-Histidine HCl monohydrate | 3.2 g |
| (L-Histidine equivalent) | 2.4 g |
| L-Arginine HCl | 7.3 g |
| (L-Arginine equivalent) | 6 g |
| Amino acids | 7.99% w/v |
| Total nitrogen | 12.2 g/L |
| Branched-chain amino acids[a] | 2.84% w/v |
| Fischer's ratio[b] | 37.05 |
| Specific gravity (20°C) | 1.025 |
| E/N ratio | 1.09 |
| $Na^+$ | about 14 mEq/L |
| $Cl^-$ | about 94 mEq/L |
| pH | 5.5-6.5 |
| Osmotic pressure[c] | about 3 |

[a]Valine + Leucine + Isoleucine (w/v %)

[b]Molar ratio of $\frac{(\text{valine} + \text{leucine} - \text{isoleucine})}{(\text{tyrosine} + \text{phenylalanine})}$

[c]Ratio to normal saline



# Composition of some amino acid solutions

| Product | Aminosol | | Amiparen | Aminoplasmal | Aminoven infant | Aminoleban | Kidmin | Nephrosteril | Dipeptiven |
|---|---|---|---|---|---|---|---|---|---|
| Volume (mL) | 500 | | 500 | 500 | 100 | 500 | 200 | 250 | 100 |
| Concentration (%w/v) | 5 | 10 | 10 | 15 | 10 | 8 | 7.2 | 7 | 20 |
| Amino acid (g/Bottle) | 25 | 50 | 50 | 75 | 10 | 40 | 14.4 | 17.5 | 20 |
| **Essential Amino Acid (g/100 mL)** | | | | | | | | | |
| Isoleucine | 0.255 | 0.51 | 0.8 | 0.585 | 0.8 | 0.9 | 0.9 | 0.51 | - |
| Leucine | 0.445 | 0.89 | 1.4 | 1.14 | 0.13 | 1.1 | 1.4 | 1.03 | - |
| Valine | 0.24 | 0.48 | 0.8 | 0.72 | 0.9 | 0.84 | 1 | 0.62 | - |
| Methionine | 0.19 | 0.38 | 0.39 | 0.57 | 0.312 | 0.1 | 0.3 | 0.28 | - |
| Threonine | 0.205 | 0.41 | 0.57 | 0.54 | 0.44 | 0.45 | 0.35 | 0.48 | - |
| Lysine | 0.35 | 0.7 | 1.05 | 0.795 | 0.851* | 0.61 | 0.5** | 0.71 | - |
| Phenylalanine | 0.255 | 0.51 | 0.7 | 0.57 | 0.375 | 0.1 | 0.5 | 0.38 | - |
| Tryptophan | 0.09 | 0.18 | 0.2 | 0.21 | 0.201 | 0.07 | 0.25 | 0.19 | - |
| Histidine | 0.26 | 0.52 | 0.5 | 0.525 | 0.476 | 0.24 | 0.35 | 0.43 | - |
| **Conditionally essential Amino Acid (g/ 100 mL)** | | | | | | | | | |
| Arginine | 0.46 | 0.92 | 1.05 | 1.605 | 0.75 | 0.6 | 0.45 | 0.49 | - |
| Cysteine | 0.036 | 0.072 | 0.1 | 0.037 | 0.052 | 0.3 | 0.1 | 0.037 | - |
| Glycine (Aminoacetic acid) | 0.395 | 0.79 | 0.59 | 1.92 | 0.415 | 0.9 | - | 0.32 | - |
| Glutamine | - | - | - | - | - | - | - | - | 13.46 |
| Proline | 0.445 | 0.89 | 0.5 | 0.735 | 0.971 | 0.8 | 0.3 | 0.43 | - |
| Tyrosine | 0.065 | 0.126 | 0.05 | 0.05 | 0.42 | - | 0.05 | - | - |
| **Dispensable Amino Acid (g/100 mL)** | | | | | | | | | |
| Alanine | 0.685 | 1.37 | 0.8 | 2.235 | 0.93 | 0.75 | 0.25 | 0.63 | 8.2 |
| Aspartic acid | 0.065 | 0.13 | 0.1 | 0.795 | - | - | 0.1 | - | - |
| Asparagine | 0.186 | 0.372 | - | - | - | - | - | - | - |
| Glutamic acid | 0.23 | 0.46 | 0.1 | 1.62 | - | - | 0.1 | - | - |
| Serine | 0.12 | 0.24 | 0.3 | 0.3 | 0.767 | 0.5 | 0.3 | 0.45 | - |
| **Others (g/100 mL)** | | | | | | | | | |
| Taurine | - | | - | - | 0.04 | - | - | - | - |
| Ornithine | 0.16 | 0.32 | - | - | - | - | - | - | - |
| Malic acid | - | | - | - | 0.262 | - | - | 0.15 | - |

*l-Lysine acetate 1.2 g, **l-Lysine acetate 0.71 g

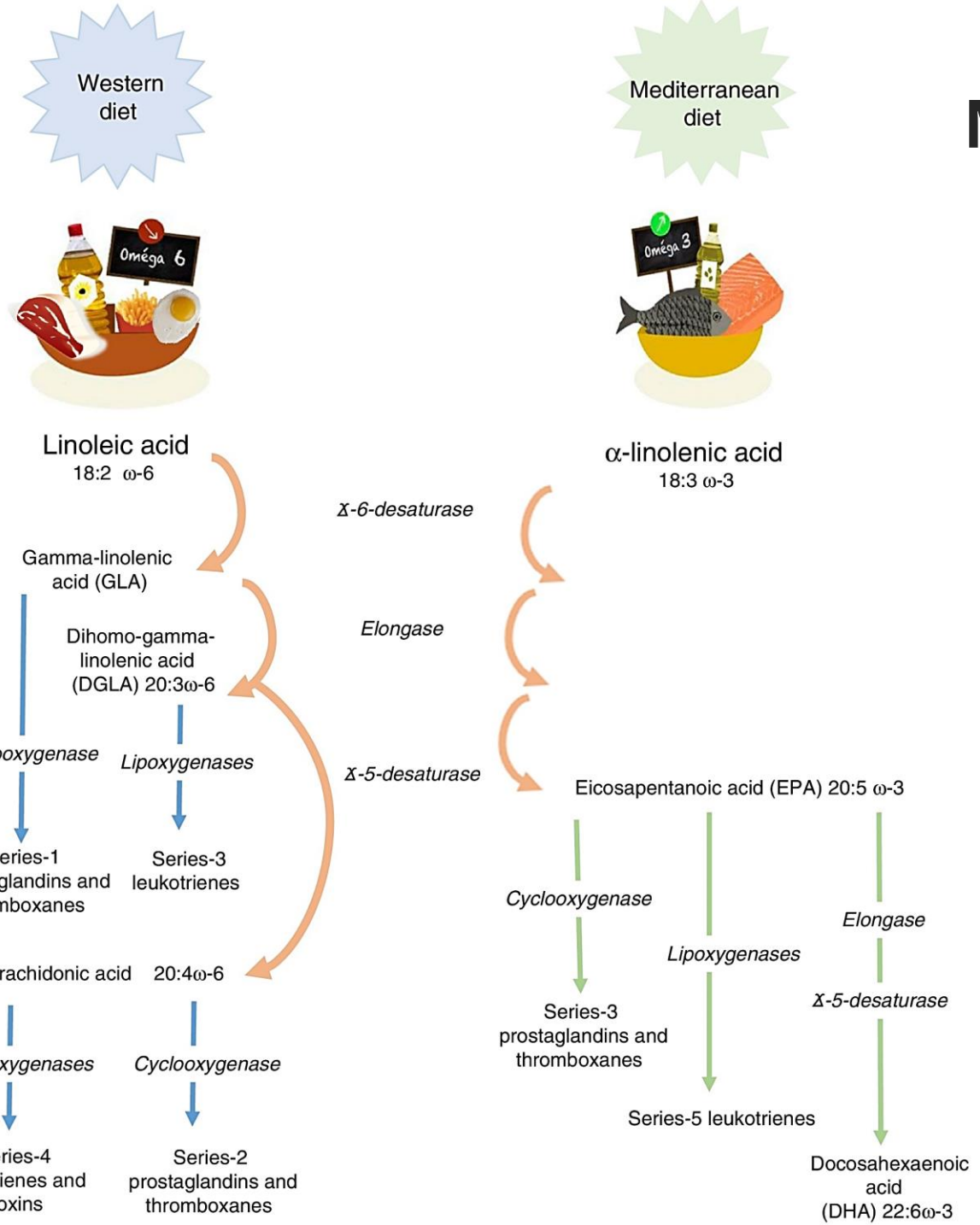
Neutral Acidic Basic

# ASPEN 2009

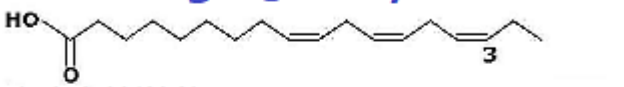
- Eicosapentaenoic acid (EPA [20:5(N-3)]) is a polyunsaturated long-chain N-3 fatty acid and a substrate for cyclooxygenase and lipoxygenase leading to eicosanoids of the 3- and 5-series, which display little or no inflammatory activity.
- EPA is a competitive antagonist of N-6 arachidonic acid, which is converted to strongly pro-inflammatory eicosanoids of the 2- and 4-series.
- N-3 long chain fatty acids are present in relatively high amounts in oily fish or are available as nutrition supplements.
- After oral intake, N-3 fatty acids are rapidly incorporated into cell membrane phospholipids
- Fish oil (most frequently used doses: 4-6 g/day) as well as long chain N-3 fatty acids (1-2 g/day) diminish inflammatory responses in cancer patients as evidenced by a decrease in inflammatory markers (interleukin 6 or C-reactive protein) and resting energy expenditure

Arends J. et al. ESPEN guidelines on nutrition in cancer patients. ***Clinical Nutrition***. 2016;1-38. http://dx.doi.org/10.1016/j.clnu.2016.07.015.

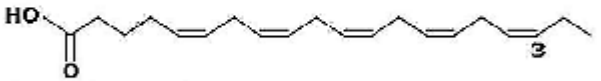
# Metabolism of linoleic acid and α-linolenic acid.



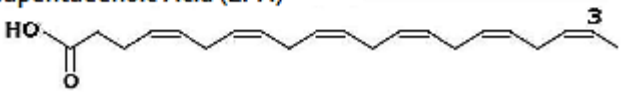

## Omega-3 fatty acids




α-Linolenic Acid (ALA)

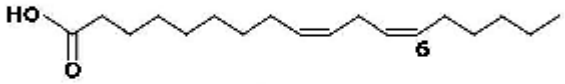



Eicosapentaeenoic Acid (EPA)

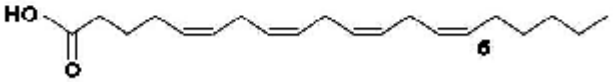



Docosahexaenoic Acid (DHA)

## Omega-6 fatty acids




Linoleic Acid (LA)




Arachidonic Acid (AA)

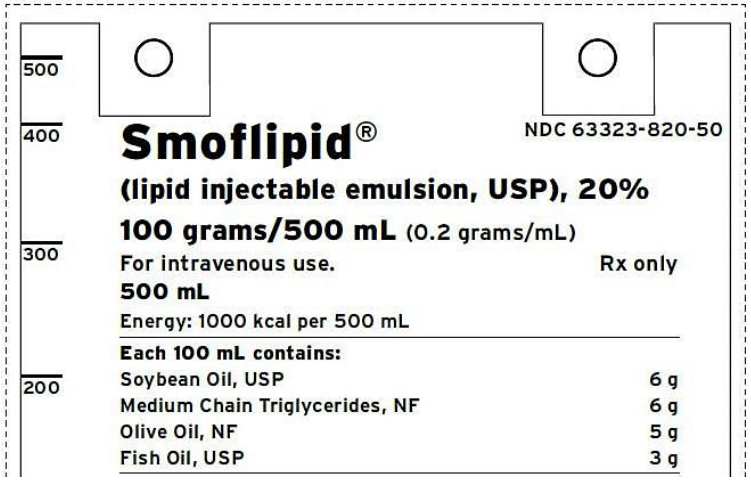
S.Huerta-Yépezetal. Role of diets rich in omega-3 and omega-6 in the development of cancer. ***Bol Med Hosp Infant Mex.*** 2016;73(6):446-456.

# ASPEN 2009




Omacor soft-gelatin cap 1000 mg

Abbott
Thai FDA Category : D
Form : Capsule
Contents : omega-3-acid ethyl esters
MIMS Class : Dyslipidaemic Agents
Color : Yellow
Shape : Oval
Size : 2.5 cm



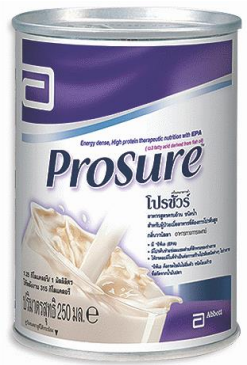
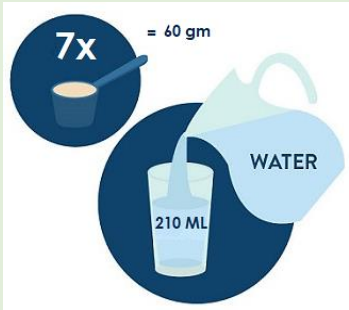
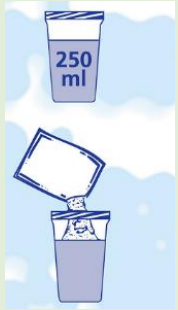
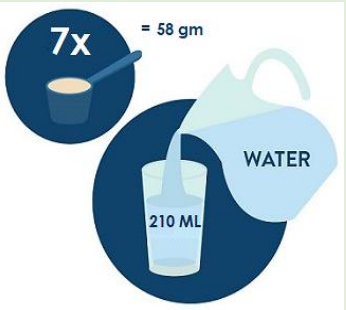
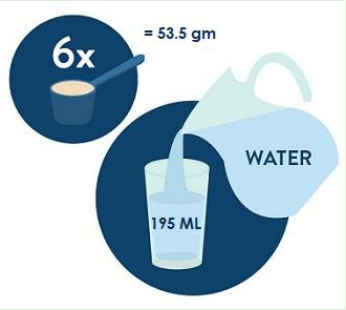

- Enteral ω-3 fatty acids appear to stabilize weight or decrease the rate of weight loss in cancer patients, although this appears to occur with little or no increase in lean body mass.
- A target dose of ***2 g of eicosapentanoic acid*** daily appears appropriate.

1. August DA et al. A.S.P.E.N. Clinical Guidelines: Nutrition Support Therapy During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation. ***J Parenter Enteral Nutr.*** 2009;33:472-500.
2. de Luis DA, Izaola O, Aller R, Cuellar L, Terroba MC. A randomized clinical trial with oral Immunonutrition (omega3-enhanced formula vs. arginine-enhanced formula) in ambulatory head and neck cancer patients. ***Ann Nutr Metab.*** 2005;49(2):95-99.

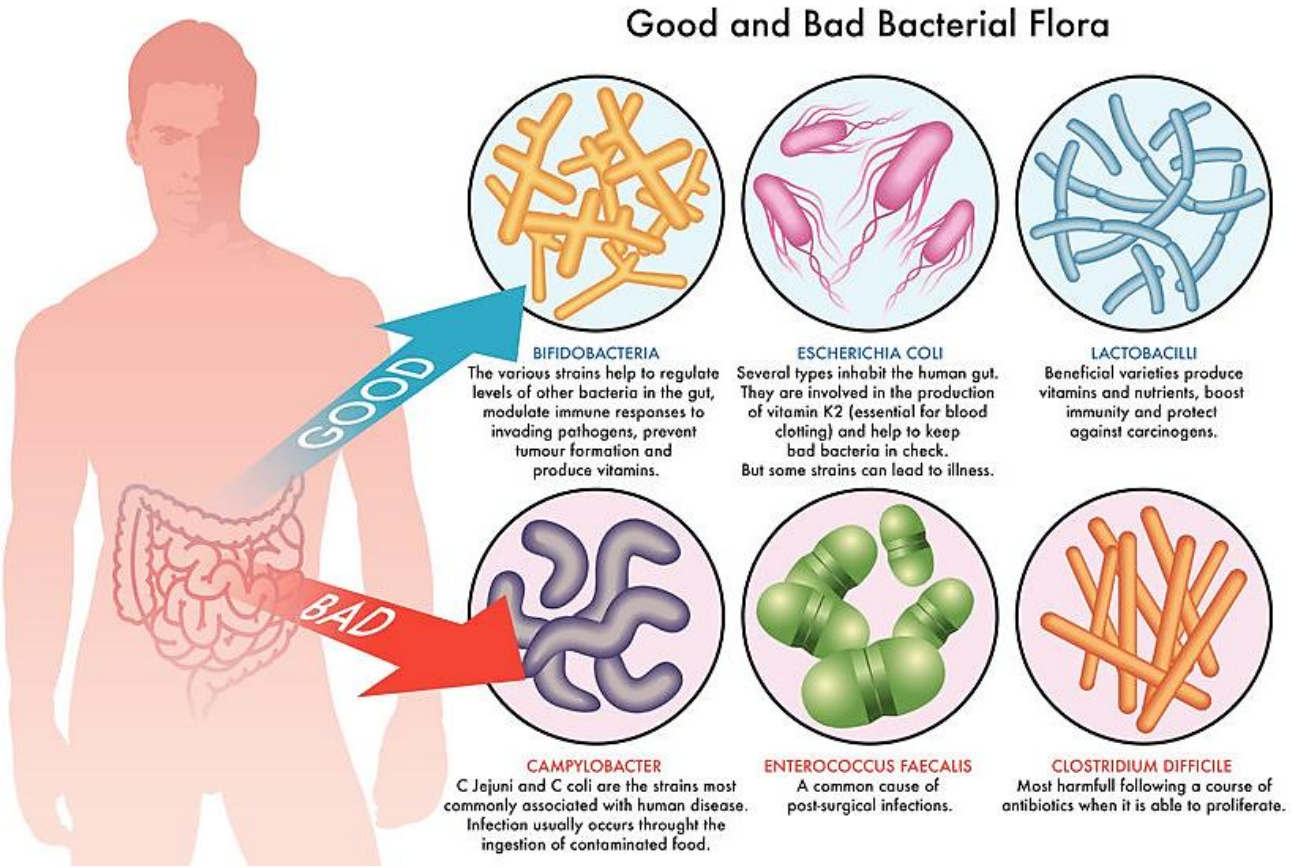
# ASPEN 2009

- Immune enhancing enteral formulas containing mixtures ***of arginine, nucleic acids, and essential fatty acids*** may be beneficial in malnourished patients undergoing major cancer operations.
- "immune enhancing" substrates including arginine, RNA, and ω-3 fatty acids have reported improved immune parameters and clinical outcomes.
- The U.S. Summit on Immune-Enhancing Enteral Therapy produced consensus recommendations regarding the use of these formulas in surgical patients.
- It was recommended that individuals undergoing gastrointestinal or major head and neck surgery in whom there is preexisting malnutrition would benefit from 5-7 days preoperative supplementation.

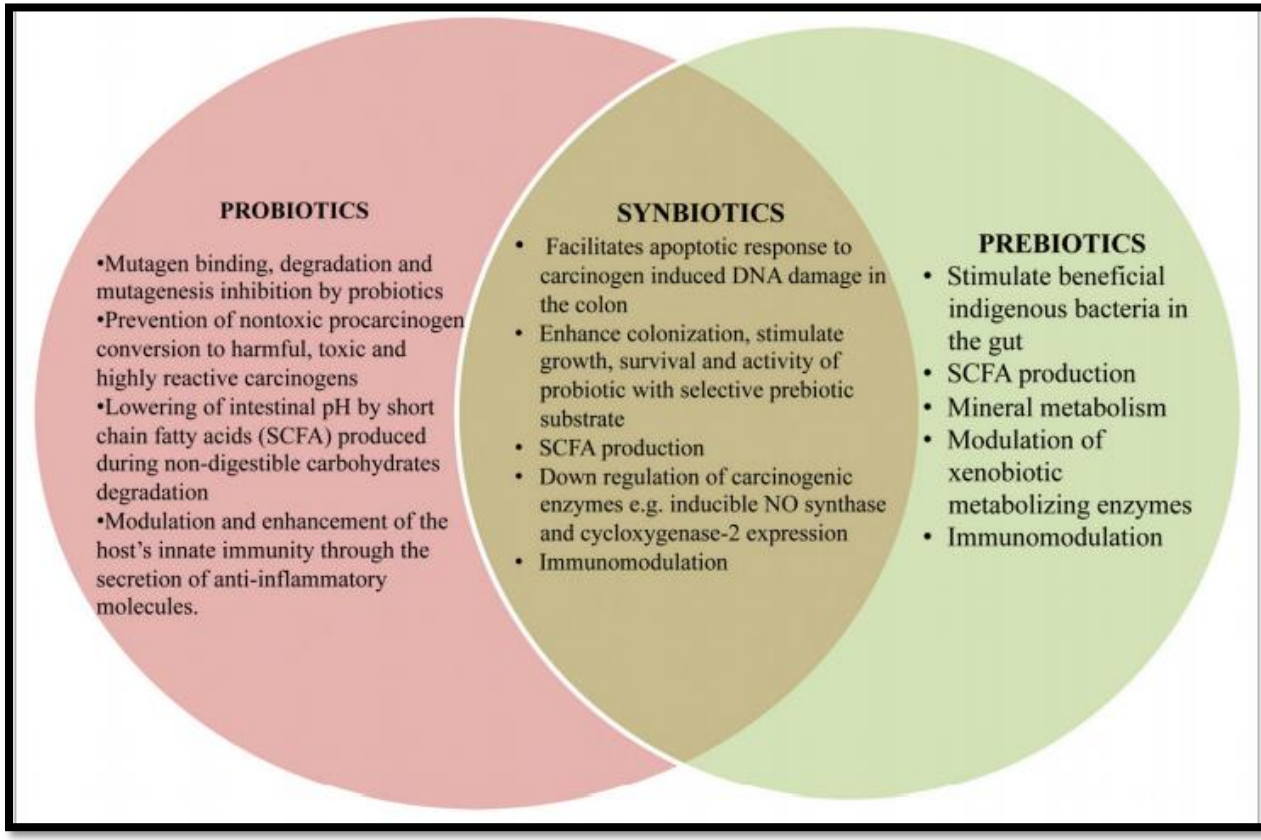
August DA et al. A.S.P.E.N. Clinical Guidelines: Nutrition Support Therapy During Adult Anticancer Treatment and in Hematopoietic Cell Transplantation. ***J Parenter Enteral Nutr.*** 2009;33:472-500.

| Product | ProSure® | Neo-mune | Oral Impact | Nutren Fiber | Forticare | Ensure |
|---|---|---|---|---|---|---|
| |  |  |  |  |  |  |
| Preparing and Remark* | Protein 21%<br>EPA 1 gm/bottle<br>Max. 3 bottles per day<br>High fiber |  <br>High Protein 25%<br>Arginine 20% + Glutamine 10% + Fish Oil 19% |  <br>Whey 100%<br>Arginine 12.5 gm/L<br>Neucleotide 1.5 gm/L |  | Whey<br>Oligofuctose, inulin, cellulose, resistant starch |  |
| Volume (mL) | 250 | 250 | 250 | 250 | 125 | 230 |
| Energy (Kcal) | 315 | 250 | 303 kCal/74 gm | 250 | 205 | 230 |
| Protein (gm/L) | 66.4 | 61.5 | 56 | 59.5 | 90.4 | 37.2 |

# Probiotics Synbiotics and Prebiotics




https://www.pakistantoday.com.pk/2018/11/18/so-whats-your-gut-feeling/




Gut Microbes 4:3, 181–192; May/June 2013; © 2013 Landes Bioscience

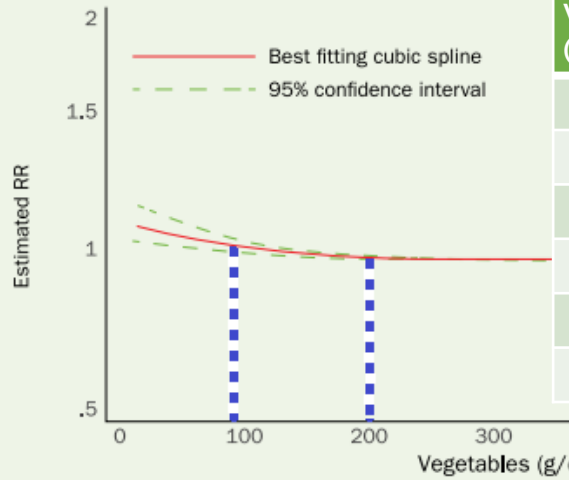

https://www.wcrf.org/dietandcancer/recommendations/limit-red-processed-meat

## WHOLEGRAINS, VEGETABLES AND FRUIT AND THE RISK OF CANCER

| WCRF/AICR GRADING | | DECREASES RISK | | INCREASES RISK | |
|---|---|---|---|---|---|
| | | Exposure | Cancer site | Exposure | Cancer site |
| STRONG EVIDENCE | Convincing | | | Aflatoxins | Liver 2015[1] |
| | Probable | Wholegrains | Colorectum 2017 | Foods preserved by salting (including preserved non-starchy vegetables) | Stomach 2016[2] |
| | | Foods containing dietary fibre | Colorectum 2017[3] | | |
| | | *Non-starchy vegetables and fruit (aggregated)* | *Aerodigestive cancer and some other cancers (aggregated)*[4] | | |
| LIMITED EVIDENCE | Limited – suggestive | Non-starchy vegetables | Mouth, pharynx and larynx 2018<br>Nasopharynx 2017<br>Oesophagus (adenocarcinoma) 2016<br>Oesophagus (squamous cell carcinoma) 2016<br>Lung (people who smoke or used to smoke tobacco) 2017<br>Breast (oestrogen receptor-negative)[8] 2017 | Non-starchy vegetables (low intake) | Colorectum 2017[5] |
| | | | | Preserved non-starchy vegetables | Nasopharynx 2017 |
| | | Fruit | Oesophagus (squamous cell carcinoma) 2016<br>Lung (people who smoke or used to smoke tobacco) 2017 | | |
| | | Citrus fruit | Stomach (cardia) 2016 | | |
| | | Non-starchy vegetables and fruit | Bladder 2015[9] | Fruit (low intake) | Stomach 2016[6]<br>Colorectum 2017[7] |
| | | Foods containing carotenoids | Lung 2017[10]<br>Breast 2017[11] | | |
| | | Foods containing beta-carotene | Lung 2017[12] | | |
| | | Foods containing vitamin C | Lung (people who smoke tobacco) 2017[13]<br>Colorectum (colon) 2017[14] | | |
| | | Foods containing isoflavones | Lung (people who have never smoked tobacco) 2017[15] | | |
| STRONG EVIDENCE | Substantial effect on risk unlikely | Beta-carotene:<br>Prostate 2014[16] | | | |

Bioactive nutrients and non-nutrient compounds: Vitamin E, selenium, copper, zinc, lignans, phytoestrogens and phenolic compounds and dietary fibre. Many of these compounds, which are largely found in the bran and germ of the grain, have plausible ***anti-carcinogenic properties.*** For instance, several phenolic acids have been shown in experimental studies to stimulate anti-oxidative activity. Alkylresorcinols, which are biomarkers of wholegrain wheat and rye intake.
Wholegrains may also protect against colorectal cancer by ***binding carcinogens and regulating glycaemic response***.

**CUP non-linear dose–response association of vegetable intake and the risk of colorectal cancer**




| Vegetable intake (Gm/day) | RR (95% CI) |
|---|---|
| 22 | 1.16 (1.11-1.21) |
| 100 | 1.08 (1.06-1.10) |
| 200 | 1.00 |
| 300 | 0.96 (0.95-0.97) |
| 400 | 0.95 (0.95-0.96) |
| 500 | 0.96 (0.96-0.96) |

**Summary of published dose–response analyses from individual cohort studies on consumption of vegetables and the risk of cancers of the mouth, pharynx and larynx**

| Cancer site | Study | Increment | No. of cases | RR (95% CI) |
|---|---|---|---|---|
| Oral cavity | Netherlands cohort study [125] | 25 g/day | 131 | 0.95 (0.89–1.02) |
| | NIH-AARP [124] | serving/1,000 kcal | 319 | 0.84 (0.73–0.95) |
| Oro- and hypopharyngeal combined | Netherlands cohort study [125] | 25 g/day | 88 | 0.94 (0.85–1.04) |
| | NIH-AARP [124] | serving/1,000 kcal | 142 | 0.90 (0.74–1.09) |
| Laryngeal | Netherlands cohort study [125] | 25 g/day | 193 | 0.98 (0.92–1.04) |
| | NIH-AARP [124] | serving/1,000 kcal | 279 | 0.91 (0.79–1.05) |
| Head and neck | Netherlands cohort study [125] | 25 g/day | 415 | 0.96 (0.92–1.01) |
| | NIH-AARP [124] | serving/1,000 kcal | 787 | 0.89 (0.82–0.97) |
| Upper aerodigestive tract | European Prospective Investigation into Cancer and Nutrition [126] | 40 g/day | 352 | 0.89 (0.78–1.02) |

## PRESERVATION AND PROCESSING OF FOODS AND THE RISK OF CANCER

| WCRF/AICR GRADING | | DECREASES RISK | | INCREASES RISK | |
|---|---|---|---|---|---|
| | | Exposure | Cancer site | Exposure | Cancer site |
| STRONG EVIDENCE | Convincing | | | Processed meat[1] | Colorectum 2017 |
| | Probable | | | Cantonese-style salted fish[2] | Nasopharynx 2017 |
| | | | | Foods preserved by salting[3] | Stomach 2016 |
| LIMITED EVIDENCE | Limited – suggestive | | | Preserved non-starchy vegetables | Nasopharynx 2017 |
| | | | | Processed meat[1] | Nasopharynx 2017<br>Oesophagus (squamous cell carcinoma) 2016<br>Lung 2017<br>Stomach (non-cardia) 2016<br>Pancreas 2012 |
| STRONG EVIDENCE | Substantial effect on risk unlikely | None identified | | | |

1 The term 'processed meat' in the CUP refers to meats transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

2 Cantonese-style salted fish is part of the traditional diet consumed by people living in the Pearl River Delta region in Southern China. This style of fish, which is prepared with less salt than is used on the northern part of China, is allowed to ferment, and so is eaten in a decomposed state. This conclusion does not apply to fish preserved (or salted) by other means. Evidence is primarily from case-control studies, there is only one cohort study.

3 The term 'foods preserved by salting' refers mainly to high-salt foods and salt-preserved foods, including pickled vegetables and salted or dried fish, as traditionally prepared in East Asia. Evidence for foods preserved by salting and stomach cancer comes from salt-preserved foods including vegetables and fish.

https://www.wcrf.org/dietandcancer/exposures/preservation-processing



Cantonese-style salted fish contains ***nitrosamines and nitrosamine precursors.***

- High levels of one such nitrosamine, ***N-nitrosodimethylamine***, found in some samples of Cantonese-style salted fish, has been shown to induce cancer development in experimental models in animals.

- Animal models have shown that high salt levels alter the viscosity of the mucous protecting the stomach and enhance the formation of N-nitroso compounds.
- In addition, high salt intake may stimulate the colonization of ***H. pylori***, the strongest known risk factor for stomach cancer.
- Finally, in animal models, high salt levels have been shown to be responsible for the primary cellular damage which results in the promotion of stomach cancer development.


- Ham, Salami, Bacon, Pastrami and some sausages (bratwursts, chorizo, frankfurters and 'hot dogs') = ***Processed meat***
- Processed meat is rich in Fat, Protein and haem iron, which can promote tumorigenesis.
- Processed meats are often cooked at high temperatures, which can lead to increased exposure to heterocyclic amines and polycyclic aromatic hydrocarbons.
- Processed meat is also a source of exogenously derived N-nitroso compounds (Nitrites or Nitrates or other preservatives are added), which may have carcinogenic potential.

- Three portions is equivalent to about 350 to 500 grams cooked weight, of red meat.
- 500 grams of cooked red meat is about equivalent to 700 to 750 grams of raw meat.

**MEAT, FISH AND DAIRY PRODUCTS AND THE RISK OF CANCER**

| WCRF/AICR GRADING | | DECREASES RISK | | INCREASES RISK | |
|---|---|---|---|---|---|
| | | Exposure | Cancer site | Exposure | Cancer site |
| STRONG EVIDENCE | Convincing | | | Processed meat[1] | Colorectum 2017 |
| | Probable | Dairy | Colorectum 2017[2] | Red meat[3]<br>Cantonese-style salted fish[4] | Colorectum 2017<br>Nasopharynx 2017 |
| LIMITED EVIDENCE | Limited suggestive | | Liver 2015<br>Colorectum 2017 | Red meat[3] | Nasopharynx 2017<br>Lung 2017<br>Pancreas 2012 |
| | | | | Processed meat[1] | Nasopharynx 2017<br>Oesophagus (squamous cell carcinoma) 2016<br>Lung 2017<br>Stomach (non-cardia) 2016<br>Pancreas 2012 |
| | | | | Foods containing haem iron[6] | Colorectum 2017 |
| | | | | Grilled (broiled) or barbecued (charbroiled) meat and fish | Stomach 2016 |
| | | Dairy products | Breast (premenopause) 2017[5] | Dairy products | Prostate 2014[7] |
| | | Diets high in calcium | Breast (premenopause) 2017<br>Breast (postmenopause) 2017 | Diets high in calcium | Prostate 2014 |
| STRONG EVIDENCE | Substantial effect on risk unlikely | None identified | | | |

1 The term 'processed meat' in the CUP refers to meats transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.
2 The evidence for dairy products and colorectal cancer includes total dairy, milk and cheese and dietary calcium intakes.
3 The term 'red meat' in the CUP refers to beef, veal, pork, lamb, mutton, horse and goat.
4 Cantonese-style salted fish is part of the traditional diet consumed by people living in the Pearl River Delta region in Southern China. This style of fish, which is prepared with less salt than is used in the northern part of China, is allowed to ferment, and so is eaten in a decomposed state. This conclusion does not apply to fish preserved (or salted) by other means. Evidence is primarily from case-control studies, there is only one cohort study.
5 The evidence for dairy products and premenopausal breast cancer includes total dairy and milk intakes.
6 The term 'haem iron' refers to iron attached to a haemoprotein, which is found only in foods of animal origin. Foods that contain haem iron include red and processed meat, fish and poultry.
7 The evidence for dairy products and prostate cancer includes total dairy, milk, cheese and yogurt intakes.

Observed inverse associations between intake of dairy products and colorectal cancer development have been largely attributed to their high calcium content. In addition to calcium, lactic acid-producing bacteria may also protect against colorectal cancer,

while the ***casein*** and ***lactose*** in milk may ↑ calcium bioavailability. Other nutrients or bioactive constituents in dairy products, such as lactoferrin, vitamin D (from fortified dairy products) or the short-chain fatty acid butyrate may also impart some protective functions against colorectal cancer, but these require much better elucidation.

**MEAT, FISH AND DAIRY PRODUCTS AND THE RISK OF CANCER**

| WCRF/AICR GRADING | | DECREASES RISK | | INCREASES RISK | |
|---|---|---|---|---|---|
| | | Exposure | Cancer site | Exposure | Cancer site |
| STRONG EVIDENCE | Convincing | | | Processed meat[1] | Colorectum 2017 |
| | Probable | Dairy products | Colorectum 2017[2] | Red meat[3]<br>Cantonese-style salted fish[4] | Colorectum 2017<br>Nasopharynx 2017 |
| LIMITED EVIDENCE | Limited – suggestive | Fish | Liver 2015<br>Colorectum 2017 | Red meat[3] | Nasopharynx 2017<br>Lung 2017<br>Pancreas 2012 |
| | | | | Processed meat[1] | Nasopharynx 2017<br>Oesophagus (squamous cell carcinoma) 2016<br>Lung 2017<br>Stomach (non-cardia) 2016<br>Pancreas 2012 |
| | | | | Foods containing haem iron[6] | Colorectum 2017 |
| | | | | Grilled (broiled) or barbecued (charbroiled) meat and fish | Stomach 2016 |
| | | Dairy products | Breast (premenopause) 2017[5] | Dairy products | Prostate 2014[7] |
| | | Diets high in calcium | Breast (premenopause) 2017<br>Breast (postmenopause) 2017 | Diets high in calcium | Prostate 2014 |
| STRONG EVIDENCE | Substantial effect on risk unlikely | None identified | | | |

1 The term 'processed meat' in the CUP refers to meats transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

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7 The evidence for dairy products and prostate cancer includes total dairy, milk, cheese and yogurt intakes.

## NON-ALCOHOLIC DRINKS AND THE RISK OF CANCER

| WCRF/AICR GRADING | | DECREASES RISK | | INCREASES RISK | |
|---|---|---|---|---|---|
| | | Exposure | Cancer site | Exposure | Cancer site |
| STRONG EVIDENCE | Convincing | | | Arsenic in drinking water[1] | Lung 2017 |
| | Probable | Coffee | Liver 2015<br>Endometrium 2013[2] | Arsenic in drinking water[1] | Bladder 2015<br>Skin (unspecified) 2017 |
| | | | | Mate[3] | Oesophagus (squamous cell carcinoma) 2016 |
| LIMITED EVIDENCE | Limited – suggestive | Coffee | Mouth, pharynx and larynx 2018<br>Skin (basal cell carcinoma [men and women] / malignant melanoma [women]) 2017 | Arsenic in drinking water[1] | Kidney 2015 |
| | | Tea | Bladder 2015 | Mate[3] | Mouth, pharynx and larynx 2018 |
| STRONG EVIDENCE | Substantial effect on risk unlikely | None identified | | | |

1 The International Agency for Research on Cancer (IARC) has judged arsenic and inorganic arsenic compounds to be carcinogenic to humans (Group 1) [2]. Drinking water contaminated with arsenic is also classed separately as a human carcinogen (Group 1) [2]. Water can become contaminated by arsenic as a result of natural deposits present in the earth, volcanic activity, or agricultural, mining and industrial practices. Countries particularly affected by higher levels of arsenic in drinking water include Bangladesh, China and India.

2 The effect of coffee on the risk of endometrial cancer is observed with both caffeinated and decaffeinated coffee so cannot be attributed to caffeine.

3 Mate, an aqueous infusion prepared from dried leaves of the plant *Ilex paraguariensis*, is traditionally drunk scalding hot through a metal straw in parts of South America. In 2016, an IARC Working Group declared that drinking very hot beverages, including mate, above 65°C is probably carcinogenic to humans (Group 2A) [3].

### Summary of published cohort studies for consumption of arsenic in drinking water and the risk of lung cancer

| Study description | Total no. of cases | Sex | RR (95% CI) | Increment/contrast |
|---|---|---|---|---|
| **High-exposure areas** | | | | |
| **Chung, 2013 South-western Taiwan cohort, 1989–1996 [66]** | 71 | Men and women | 1.47 (0.66–3.31) | ≥ 19.5 vs < 9.1 µg/litre/year |
| | 43 | Men | SMR 6.05 (4.38–8.15) | |
| | 28 | Women | SMR 7.18 (4.77–10.38) | |
| **Chen, 2010 North-eastern Taiwan cohort [68]** | 178 | Men and women | 2.08 (1.33–3.27) | ≥ 10,000 vs < 400 µg/litre/year |
| **Tsuda, 1995 Japanese cohort, 1959–1992 [67]** | 9 | Men and women | SMR 15.69 (7.38–31.02) | ≥ 1 ppm |
| **Low-exposure areas** | | | | |
| **Baastrup, 2008 Danish Diet, Cancer and Health cohort [69]** | 402 | Men and women | IRR 0.99 (0.90–1.08) | Per 1 µg/litre |
| | | | IRR 1.00 (0.98–1.03) | Per 5 mg/litre |

### Summary of published cohort studies for consumption of arsenic in drinking water and the risk of skin cancer

| Study description | Total no. of cases | Sex | RR (95% CI) | Increment/contrast |
|---|---|---|---|---|
| **High-exposure areas** | | | | |
| **Hsueh, 1997 South-western Taiwan cohort 1989–1992 [78]** | 26 | Men and women | Skin cancer 8.69 (1.08–65.50) | 0.71–1.1 vs 0 mg/litre |
| **Low-exposure areas** | | | | |
| **Baastrup, 2008 Danish Diet, Cancer and Health cohort [69]** | 147 | Men and women | Malignant melanoma IRR 0.80 (0.59–1.08) | Per 1 µg/litre Time-weighted average exposure |
| | | | Non-melanoma skin cancer IRR 0.99 (0.94–1.06) | Per 1 µg/litre Time-weighted average exposure |
| **Lewis, 1999 Cohort of Mormons, USA[1] [75]** | 3 | Men | Malignant melanoma SMR 0.83 (0.17–2.43) | ≥ 5,000 vs <1,000 ppb-years |
| | 4 | Women | Malignant melanoma SMR 1.82 (0.50–4.66) | |

# Keto Diet for Cancer

# Keto diet

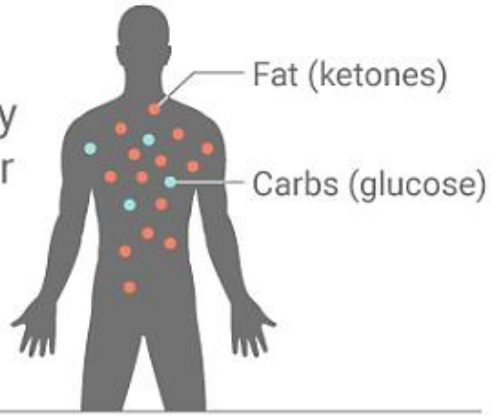


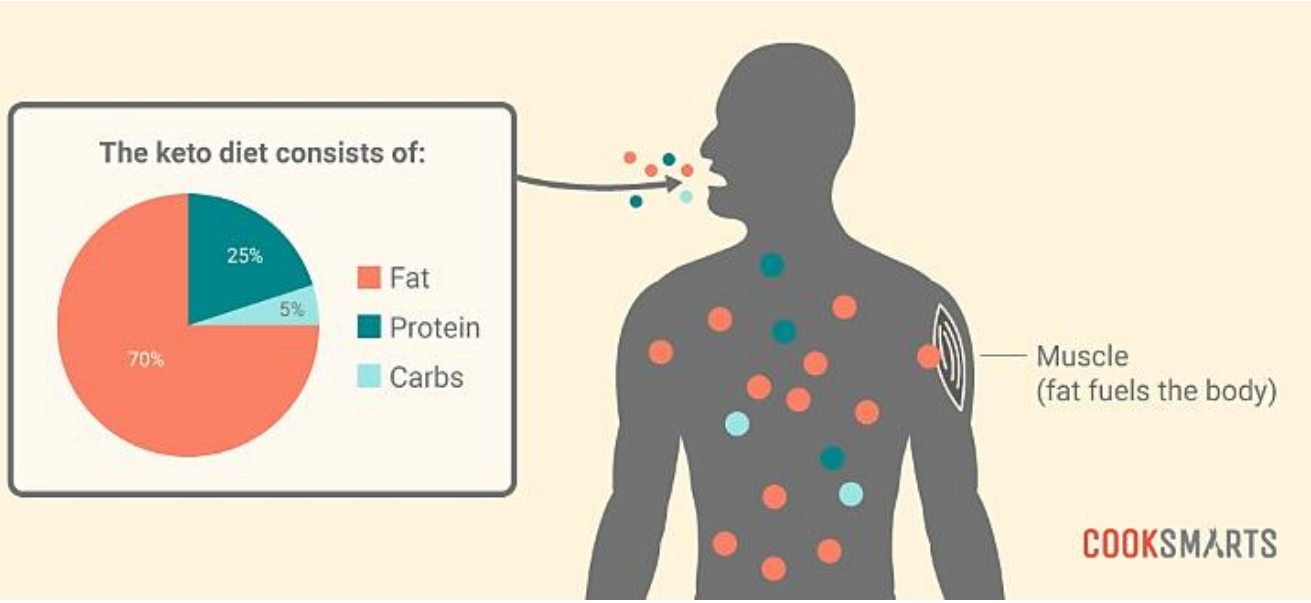
## What is Ketosis?

Ketosis is the metabolic process during which the body shifts from burning carbohydrates (glucose) for fuel to burning fat (ketones).

## How Do You Get into Ketosis?

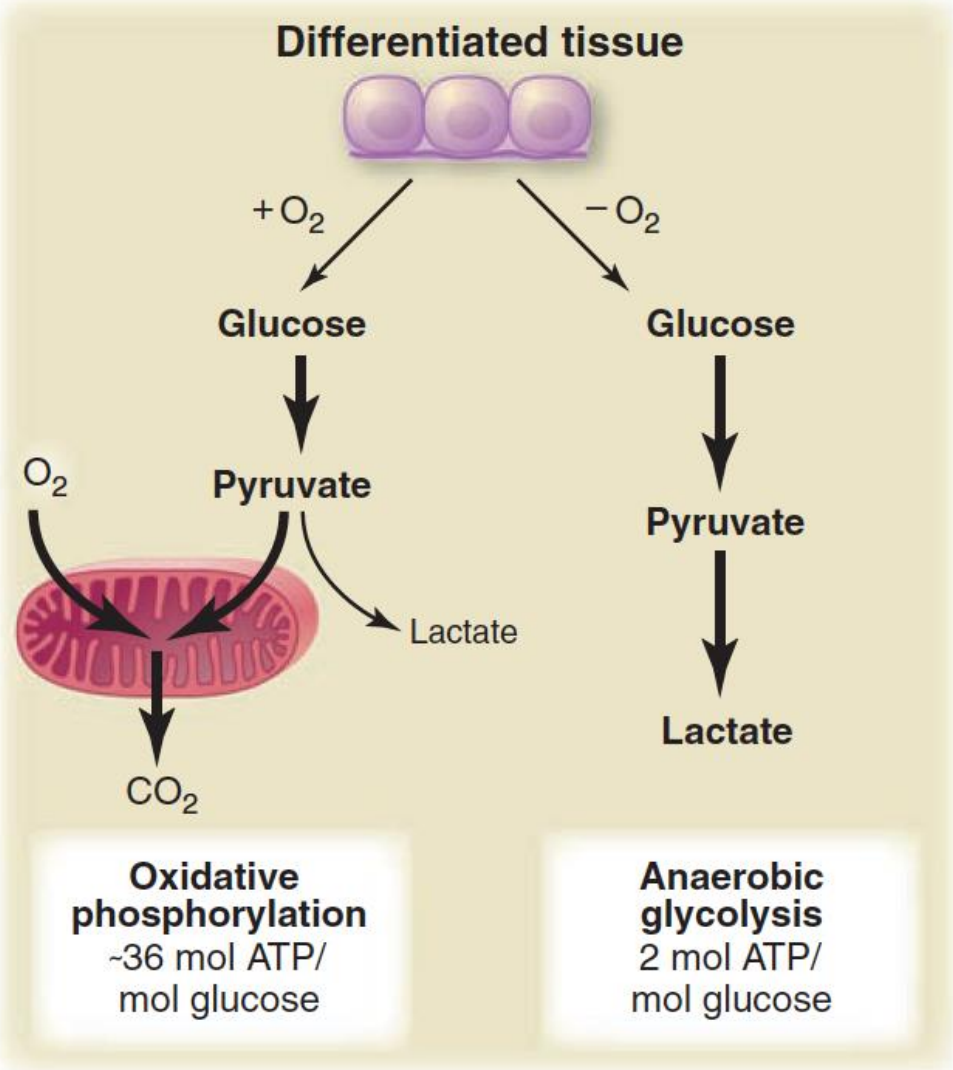
By eating more fat and significantly reducing carbs, you can cause your body to use up its glucose stores and enter into a state of ketosis.

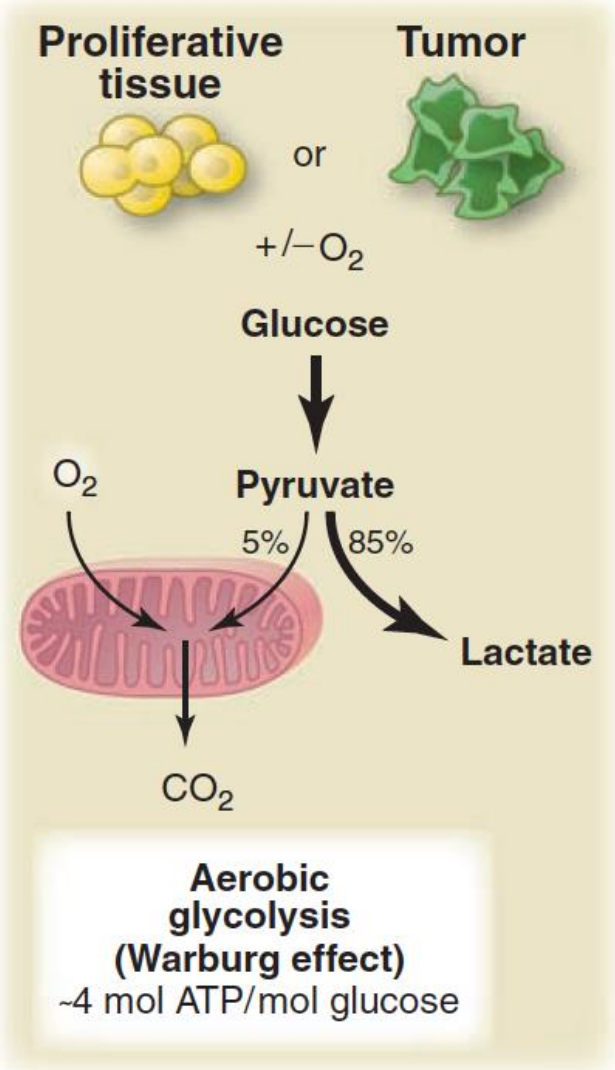


# Energy Pathways of Normal and Cancer Cells



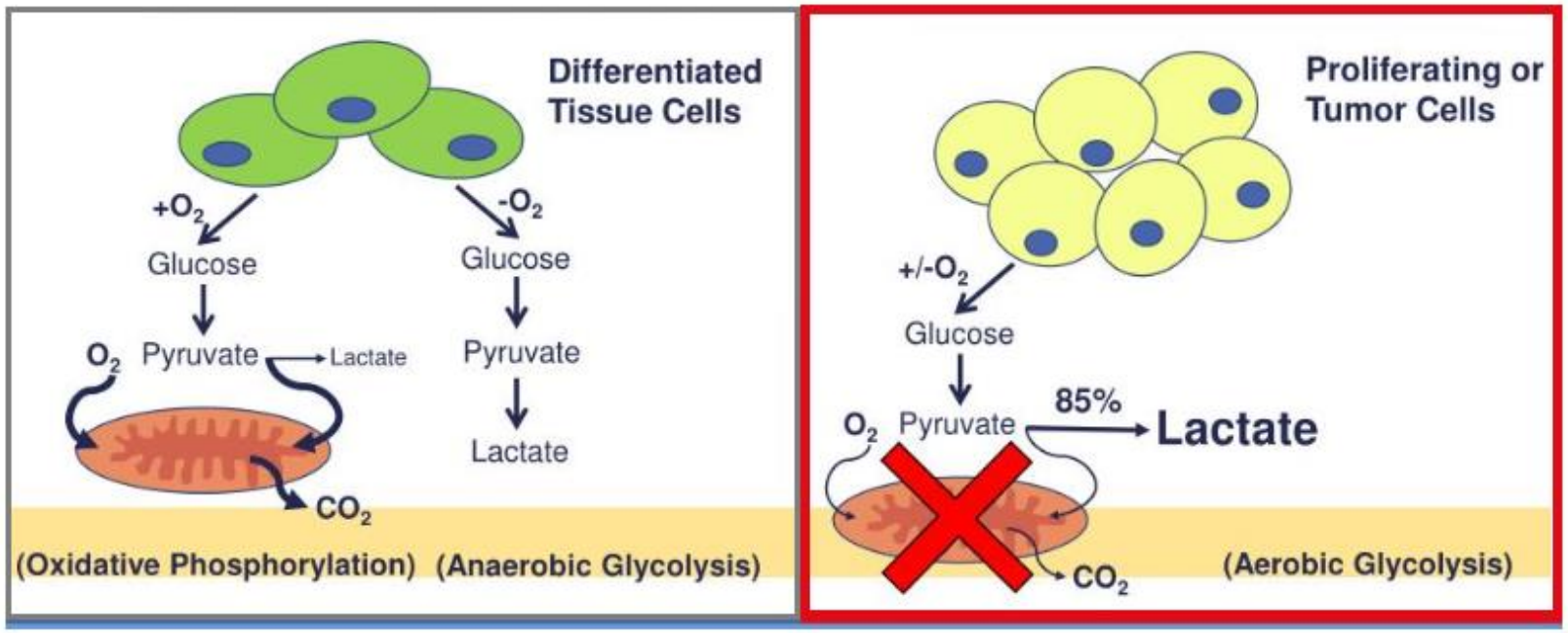


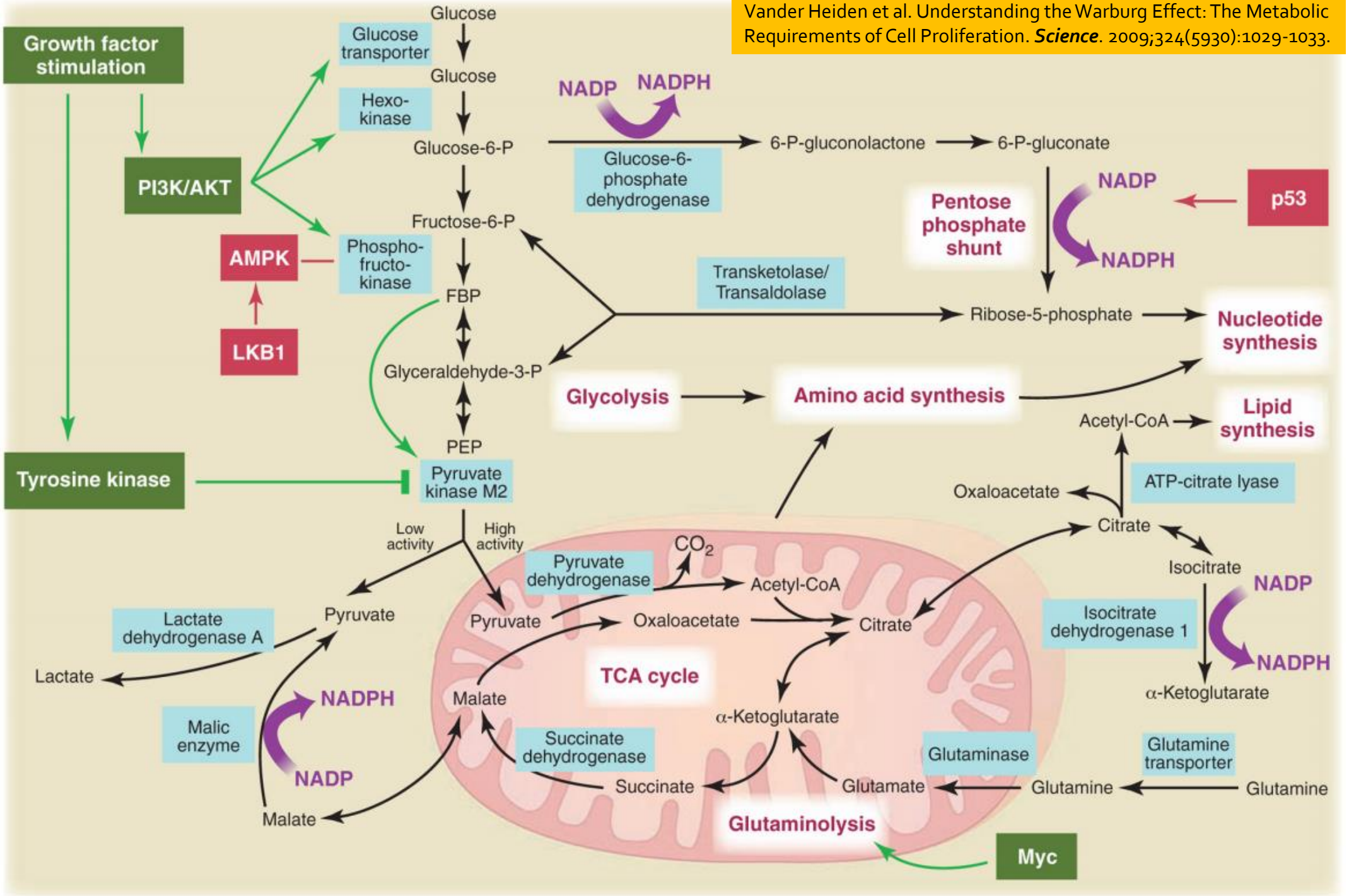

- Glycolysis generates 2ATP, while oxidative phosphorylation generates 36-38ATP.
- Despite that most cancer cells have been found to exclusively produce their energy via the glycolytic pathway regardless of the level of oxygen in the surroundings.
- A possible reason for this I that the glycolytic pathway enables the production of specific metabolites (NADPH) that decrease the presence of ROS species/oxidative stress.
- This  crucial for tumor cells as it allows them to proliferate indefinitely and survive I "unfavorable condition"

# Energy Pathways of Normal and Cancer Cells





Vander Heiden et al. Understanding the Warburg Effect: The Metabolic Requirements of Cell Proliferation. ***Science***. 2009;324(5930):1029-1033.



# Ketogenic Diet

**Tumor and Tumor microenvironment**
- ↓Glucose
- ↓Insulin
- ↑Ketones
- ↓Glucose: Ketone Index
- ↑ Modulation of Gene Expression via HDACI

**↓ Intermediate endpoint biomarkers of Inflammation, Oxidative stress, angiogenesis, metabolic dysregulation in the tumor and tumor micro environment**

## Inflammation
- ↓ Inflammatory Biomarkers
- ↓ NF-KB
- ↑ Neuro-inflammation
- ↑ Anti-tumor Immunity

## Oxidative Stress
- ↑ Transcriptional activation of oxidative stress resistance factors
- ↓ Basal Free Radicals and Oxidative Stress
- ↓ Oxidative Damage

## Metabolic Regulation
- ↓ Glucose uptake and glycolysis
- ↓ GLUT1 & 3
- ↑ Ketone metabolism
- ↓ Insulin, IGF signaling
- ↓ Lactate → ↓ Acidity

## Angiogenesis
- ↓ Expression of Angiogenic factors
- ↓ MMP-2, EGFR-2, Vimentin

**↓ Tumor Progression**
**Enhanced Neuroprotection**
**↓ Symptom Burden**
**↓ Seizure Activity**
**↓ Cognitive Impairment**
**Improved Overall HRQOL**

# Cancer and Keto Diet

## Foods to Eat on a Keto Diet

**Healthy fats and oils**
Butter, lard, coconut oil, olive oil, and high-fat dressings.

**Dairy**
Full-fat cheeses, sour cream, and heavy cream.

**Protein**
Eggs, beef, pork, chicken, and seafood.

**Vegetables**
Dark leafy greens like spinach and bok choy as well as other above-ground vegetables.

**Fruits**
Lower-carb fruits like blackberries, raspberries, and strawberries.

**Nuts and seeds**
Macadamia nuts, pecans, and almond butter are excellent high-fat options.

## Foods Not to Eat on a Keto Diet

**Starchy vegetables**
Vegetables that grow underground like potatoes are high in carbs.

**Pastas, breads, rice, and cereals**
These are carb-heavy foods that should be avoided.

**Fruits**
High-carb fruits like bananas, grapes, and mangos.

**Ultra processed foods**
Chips, margarine, TV dinners, crackers, low-fat anything.

**Milk**
Milk, even full-fat milk, contains lactose (sugars).

**Sweets**
Candy and cakes.

# Ketogenic Diet Plan For Cancer Patient


# Nutritional Supplements) and Cancer

- **Beta-carotene** increases risk of **Lung cancer** (RR 1.16 [1.06 to 1.27]) and **stomach cancer** (RR 1.34 [1.06 to 1.7])
- **Vitamin E** increases **Prostate cancer** (RR 1.17 [1.00 to 1.36]) and **Colorectal** adenoma (RR 1.74 [1.09 to 1.79])
- **Selenium** reduced **Lung cancer** in populations with **low selenium status** (serum < 106 ng/mL), increased rates in those with higher serum levels (serum > 126 ng/mL), and reduced gastric cancer occurrence (RR 0.59 [0.46 to 0.75])
- A recent meta-analysis of randomized trials reported **increased overall mortality** with **Beta-carotene** (RR 1.05 [1.01 to 1.09]) and **Vitamin E (**RR 1.03 [1.00 to 1.05]) and **Higher doses of vitamin A**. Neither vitamin C (RR 1.02 [0.98 to 1.07]) nor selenium (RR 0.97 [0.91 to 1.03]) were beneficial, (RR 1.0006 [1.0002 to 1.001] P = 0.002).



Harvie M. American Society of Clinical Oncology educational book / ASCO. 2014;34:e478-486.

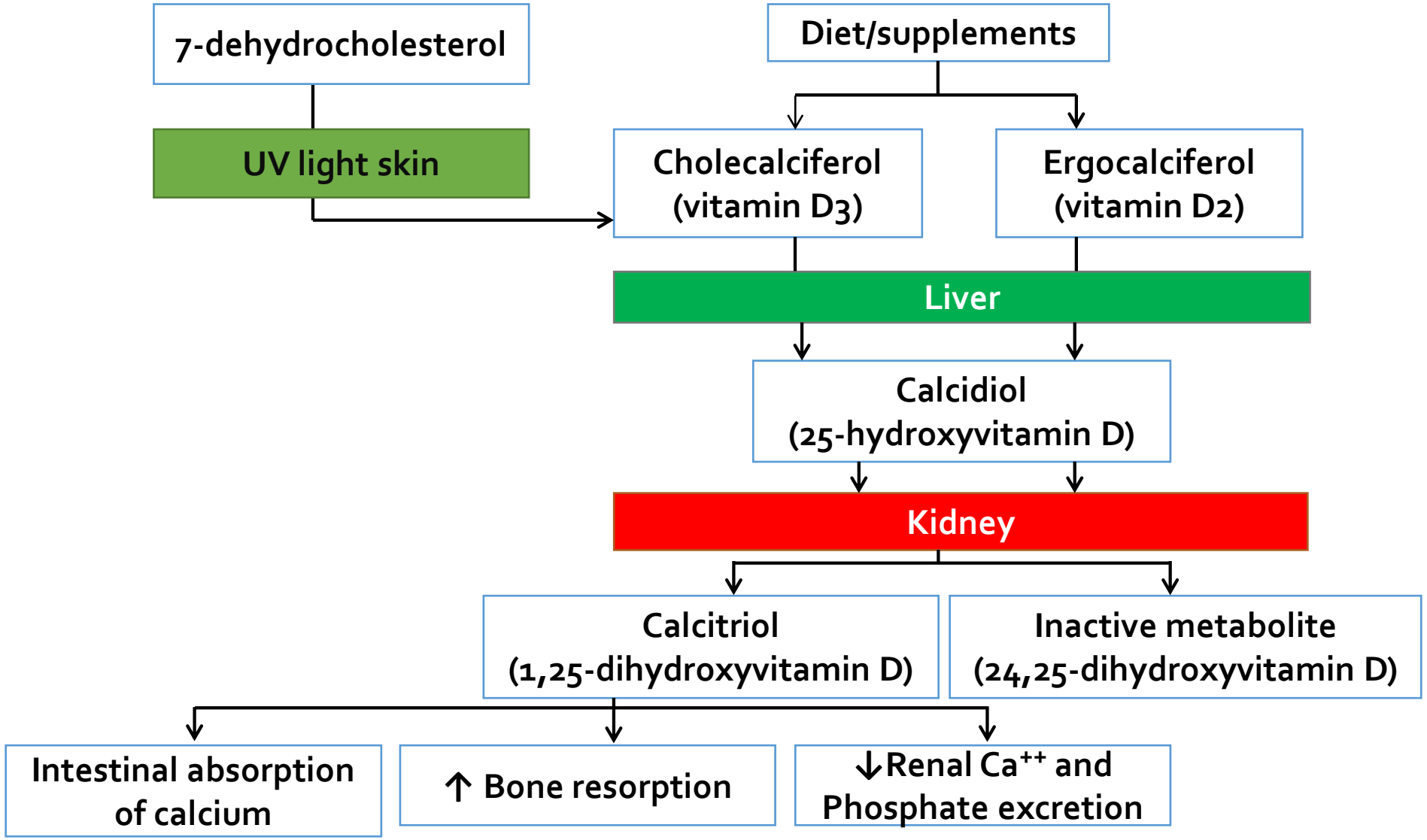

# Curcumin (Turmeric)

- Curcuminoids: curcumin
- Phytoestrogen, neuroprotective, anti-inflammatory, immunomodulatory, chemoprotective effect
- Herb-Drug interaction: Doxorubicin, Cyclophosphamide (inhibit chemotherapy-induced apoptosis via JNK pathway)


# Vitamin D

- Vitamin D3: Cholecalciferol
  - is produced intrinsically in human and animal skin when exposed to UVB light. Wool sources of 7-dehydrocholesterol are used (from cholesterol), and irradiatied to form active vitamin D3.
  - Vegetarians or especially vegans may be opposed to the use of vitamin D3 supplementation because it is derived from an animal source
  - Most healthy fish contain vitamin D3.
- Vitamin D2: Ergocalciferol
  - is synthetically made from radiating a compound (ergosterol) from the mold ergot

# Pathways of vitamin D synthesis




# Vitamin D

- Normal range: 25-OH Vitamin D 35-40 ng/mL
- 2.5 mcg (micrograms) = 100 IU
- The minimum requirement : 400 to 800 IU in adult

| Dose per day | Increase vitamin D blood level |
|---|---|
| 100 IU (2.5 mcg) | 1 ng/ml (2.5 nmol/L) |
| 200 IU (5 mcg) | 2 ng/ml (5 nmol/L) |
| 400 IU (10 mcg) | 4 ng/ml (10 nmol/L) |
| 500 IU (12.5 mcg) | 5 ng/ml (12.5 nmol/L) |
| 800 IU (20 mcg) | 8 ng/ml (20 nmol/L) |
| 1000 IU (25 mcg) | 10 ng/ml (25 nmol/L) |

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Clinical Oncology Pharmacy Symposium (COPS) ครั้งที่ 12
Myth and fact in oncology
22-23 สิงหาคม 2562



Pro & Con?

Con

# คนไข้มะเร็ง ไม่ควรกินน้ำเต้าหู้

■ นพ.สมยศ กิตติมั่นคง
สำนักโรคติดต่อนำโดยแมลง กรมควบคุมโรค กระทรวงสาธารณสุข

**ตอนที่ผมออกมาบอกว่า คนไข้มะเร็งไม่ควรกินน้ำเต้าหู้ เพราะจะทำให้มะเร็งลามได้ไว และคนไข้จะตายเร็วขึ้น ทำให้เกิดคำถามย้อนกลับมาหาผมมากมายว่ามันเป็นไปได้ยังไง คนไข้ที่เจ็บป่วย ไม่ว่าโรคอะไรก็แล้วแต่ ทั้งญาติและโรงพยาบาล จะพยายามให้หาอาหารมาให้คนไข้กิน ให้ครบ 5 หมู่ให้จงได้ และน้ำเต้าหู้ หรืออีกชื่อหนึ่งก็คือ น้ำนมถั่วเหลือง ก็เป็นอาหารยอดนิยม ที่คนไข้มักจะได้กินกัน แถมยังใส่น้ำตาลผสมเพิ่มลงไปเพื่อเป็นอาหารให้กับเซลล์มะเร็งอีกด้วย**

ผมเคยไปบรรยายเรื่องการดูแลสุขภาพให้กับเจ้าหน้าที่สำนักงานอาหารและยาแห่งหนึ่ง ระหว่างการบรรยายผมก็ยกตัวอย่างเรื่องน้ำเต้าหู้ว่า จะทำให้มะเร็งลุกลามไวขึ้น นอกจากนี้ คนไข้ที่เป็นโรคเรื้อรังที่มีการอักเสบตามร่างกายเช่น ซูมาตอยด์ เอสแอลอี เป็นต้น ไม่ควรจะกินน้ำเต้าหู้เช่นกัน เพราะมันจะทำให้อาการทรุดลง ทั้งได้จังหวะช่วงพักเที่ยง ที่มีเจ้าหน้า ผมก็งง ตรงกันกับที่ผม ที่ลองทบทวนดู ที่จำได้ ไปบำรุงร่างกายด้วยน้ำเ

บางท่านถามผมว่า อยู่ในถั่วเหลืองเหรอ ที่ มากยิ่งขึ้น ไม่ใช่เหรอกครั ฐานของการออกของเซล มะเร็งเป็นเซลล์ที่กระหา มีความผิดปกติในการใ พลังงานที่เท่ากันต่อกา นั้น มันต้องได้รับพลังง พวกมัน ถ้าเส้นเลือดลง จำนวนได้ยาก เพราะเซ





นักวิทยาศาสตร์ไปพบครับว่า การที่จะเกิดเส้นเลือดงอกใหม่ หรือที่เรียกว่า neo-vasculariza ได้นั้น มันต้องได้รับแร่ธาตุชนิดหนึ่งให้เพียงพอ เค้าได้ไขมครับว่า แร่ธาตุตัวนั้นคือจะไปส่วนใหญ่จะเค้ากินไม่ลูกครับ แร่ธาตุตัวนั้นคือ ทองแดง หรือ copper นั่นเอง มีการวิจัยพบว่า ถ้าเราทำ chelation คือเอาทองแดงให้ออกจากร่างกาย ให้ต่ำลงจนถึงระดับหนึ่ง เซลล์มะเร็งก็จะหยุดนิ่ง ไปต่อไม่เป็น

ยาที่ใช้ในการดึงทองแดงออกจากร่างกาย ก็เป็นยาตัวเดียวกับที่เราใช้รักษาโรค Wilson disease ครับนอกจากยา หรือการทำ chelation เพื่อหยุดการแพร่กระจายของมะเร็งแล้ว อาหารก็เป็นส่วนสำคัญในการหยุดการแพร่กระจายของมะเร็งเช่นกัน เป็นที่น่าลงสารคนใช้มาก เพราะว่า แพทย์มักจะไม่ค่อยใส่ใจเรื่อง อาหารเป็นยา แต่มักจะสนใจทำ ยาให้เป็นอาหาร คือ คนไข้ต้องกินยา แล้วก็ไปกินอาหารให้ครบ 5 หมู่

ผมขอย้ำอีกครั้งครับว่า อาหารมีส่วนสำคัญในการรักษาโรค ไม่ใช่แค่เฉพาะโรคมะเร็ง แต่อีกหลายโรคเช่น โรคเส้นเลือดหัวใจตีบ เป็นต้น ขอสรุปง่ายๆ เลยแล้วกันนะครับว่า เราต้องพยายามอย่าให้อาหารที่มีส่วนประกอบของทองแดงให้กับผู้ป่วยโรคมะเร็ง เพราะมันจะทำให้โรคมะเร็งลุกลามหนักขึ้น ผมแบ่งอาหารเป็น 6 กลุ่ม หรือ 6 ประเภท เพื่อที่คนไข้และญาติจะได้จำง่ายๆว่า อะไรที่ไม่ควรกิน

กุ้ง
หอย
ปู
ปลาหมึก
เครื่องใน
น้ำเต้าหู้

อาหารทั้ง 6 ประเภท ข้างต้นนี้ มีทองแดงสูงครับ เป็นลำดับต้นๆเลย ดังนั้น จะยืดชีวิตของผู้ป่วยโรคมะเร็ง ต้องหยุดอาหารพวกนี้ด้วยครับ



MYFOODDATA

## Top 10 Foods Highest in Copper

0.9mg of Copper = 100% of the Daily Value (%DV)

### 1 Oysters

419% DV (3.8mg) copper
**per 6 oysters**

**493% DV** (4.4mg)
**per 100 grams**

### 2 Shiitake Mushrooms

144% DV (1.3mg) copper
**per cup cooked**

**100% DV** (0.9mg)
**per 100 grams**

### 3 Firm Tofu

106% DV (1mg) copper
**per cup**

**42% DV** (0.4mg)
**per 100 grams**

### 4 Sweet Potatoes

79% DV (0.7mg) copper
**per cup mashed**

**31% DV** (0.3mg)
**per 100 grams**

### 5 Sesame Seeds

78% DV (0.7mg) copper
**per oz**

**274% DV** (2.5mg)
**per 100 grams**

### 6 Cashews (Dry Roasted)

70% DV (0.6mg) copper
**per 1 oz handful**

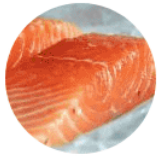
**247% DV** (2.2mg)
**per 100 grams**

### 7 Chickpeas (Garbanzo Beans)

64% DV (0.6mg) copper
**per cup**

**39% DV** (0.4mg)
**per 100 grams**

### 8 Salmon



61% DV (0.5mg) copper
**per 6oz fillet**

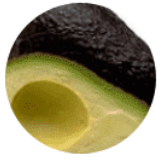
**36% DV** (0.3mg)
**per 100 grams**

### 9 Dark Chocolate (70-85% Cocoa)

56% DV (0.5mg) copper
**per 1oz square**

**196% DV** (1.8mg)
**per 100 grams**

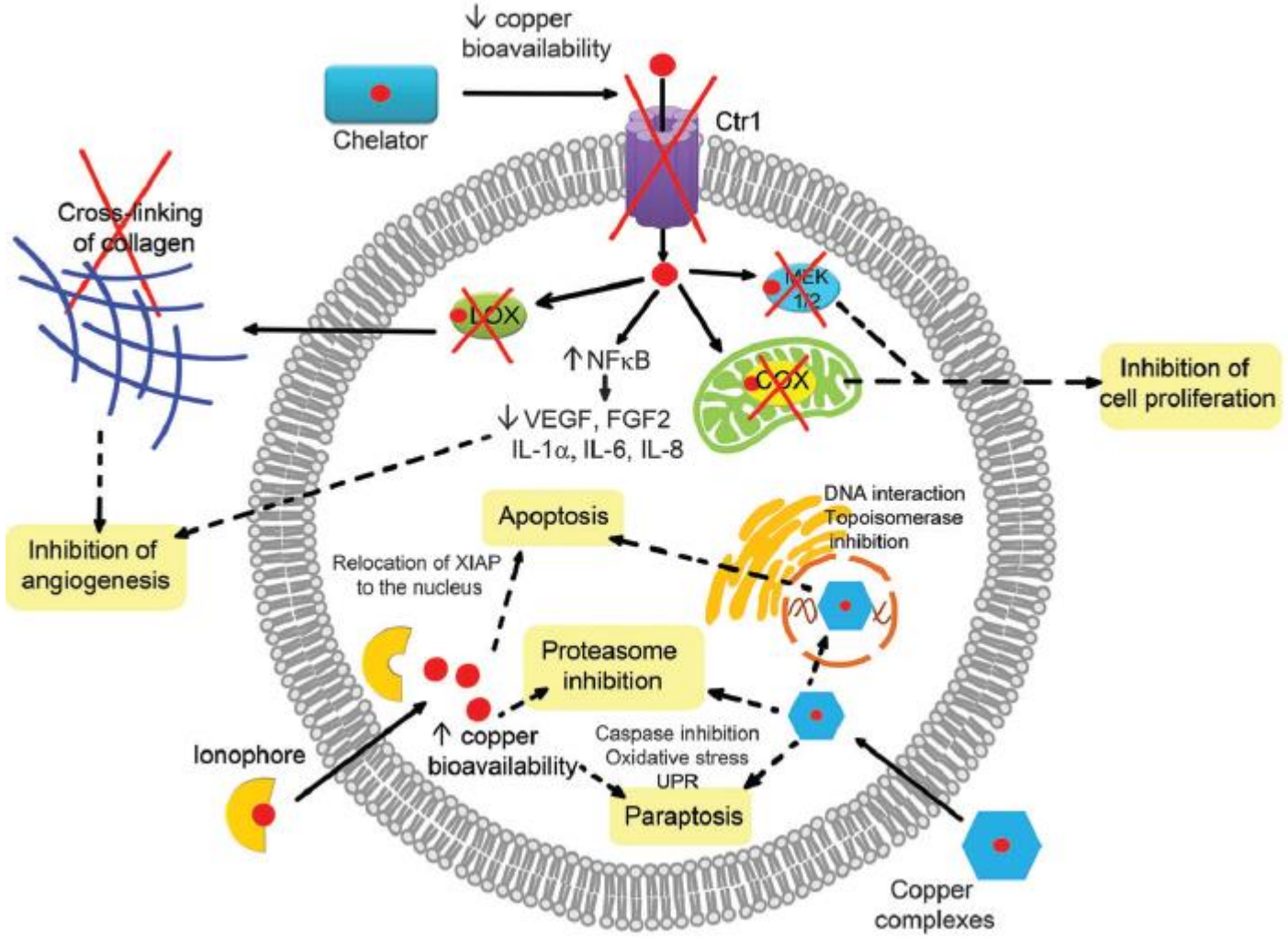
### 10 Avocados



42% DV (0.4mg) copper
**per avocado**

**21% DV** (0.2mg)
**per 100 grams**

# Copper coordination compounds target




Denoyer, D., Masaldan, S., La Fontaine, S., & Cater, M. A. (2015). *Targeting copper in cancer therapy: "Copper That Cancer." Metallomics, 7(11), 1459–1476.* doi:10.1039/c5mt00149h

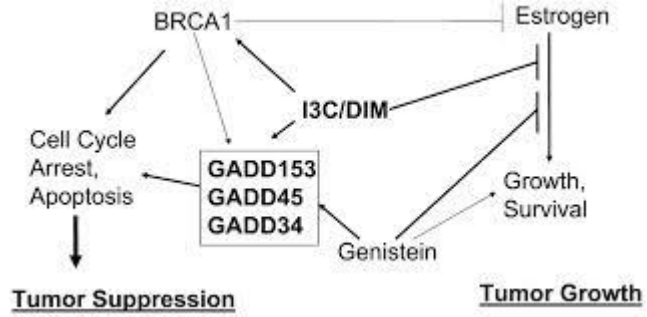

# AHCC

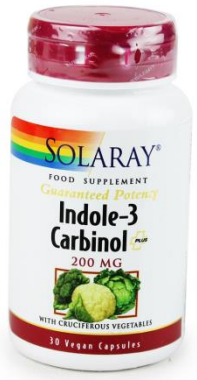

- **A**ctive **H**exose **C**orrelated **C**ompound
- Extracted from Shitake mushroom: Oligosaccharide 74% (20% acetylated alpha-1,4 glucans)
- An immunomodulatory agent
  - Enhanced NK cell activity due to an increase of NK cell granularity and binding capacity to tumor cell targets
  - Dose: 3-6 g/day ⇧ specific innate immunity in 4 weeks
  - AHCC is a substrate and inducer of CYP450 2D6 (Doxorubicin)


1. Yin Z, Fujii G, Walshe T. Effects of active hexose correlated compound on frequency of $CD_4$+ and CD8+ T cells producing interferon-γ and/or tumor necrosis factor-α in healthy adults. ***Hum Immurol.*** 2010;71(12):1187-90.
2. Mach CM, Fugii H, Wakame K, Smith J. Evaluation of active hexose correlated compound hepatic metabolism and potential for drug interactions with chemotherapy agents. ***Soc Integr Oncol*** . 2008;6(3):105-109.
3. Matsui K, Kawaguchi Y, Ozaki T, et al. Effect of active hexose correlated compound on the production of nitric oxide in hepatocytes. ***JPEN J Parenter Enteral Nutr*** . 2007;31(5):373-380; discussion 380-381.

# Indole-3-Carbinol (I3C)

- Specific compound in cruciferous vegetables: broccoli, cabbage, cauliflower
- Chemopreventive agent for breast cancer through its estrogen receptor
- Reduced cell proliferation and apoptosis and cell cycle arrest at G0/G1 phase
- CYP450 1 family inducer





# Cordyceps

- Fungus that grows on the larvae of caterpillar ***Hepialus armoricanus*** Oberthuer.
- Both are contained in the product and both are consumed
- Cordyceps in used for a wide range of conditions including fatigue, sexual dysfunction, coughs and  as adaptogen or immune stimulant
- Cordyceps stimulates the number of T helper cells, prolongs the survival of lymphocytes, enhances TNF-alpha and interleukin-1 production and increases the activity of natural killer cells in the cultured rat Kupffer cells

Jung *et al. BMC Complementary and Alternative Medicine* (2019) 19:77
https://doi.org/10.1186/s12906-019-2483-y

BMC Complementary and Alternative Medicine

RESEARCH ARTICLE Open Access

## Immunomodulatory effects of a mycelium extract of Cordyceps (Paecilomyces hepiali; CBG-CS-2): a randomized and double-blind clinical trial

Su-Jin Jung[1,4], Eun-Soo Jung[1], Eun-Kyung Choi[1,4], Hong-Sig Sin[2], Ki-Chan Ha[3] and Soo-Wan Chae[1,4,5*]

The major components of CBG-CS-2 in this study, ***Cordyceps PS and adenosine***, play an important role in presenting immune reactions as a trigger and induce an immunomodulatory effect by enhancing both the NK-cell activity and phagocyte reactions via the activation of macrophages.


# Cordyceps

- Herb-Drug interaction
  - Hypoglycemics/Insulin: Cordyceps may have additive hypoglycemic effects
  - Anticoagulant/ Antiplatelets: Cordyceps inhibits platelet arrogation and may increase the effects of these drugs
- Dosing: 3-6 g/day (for CRF)

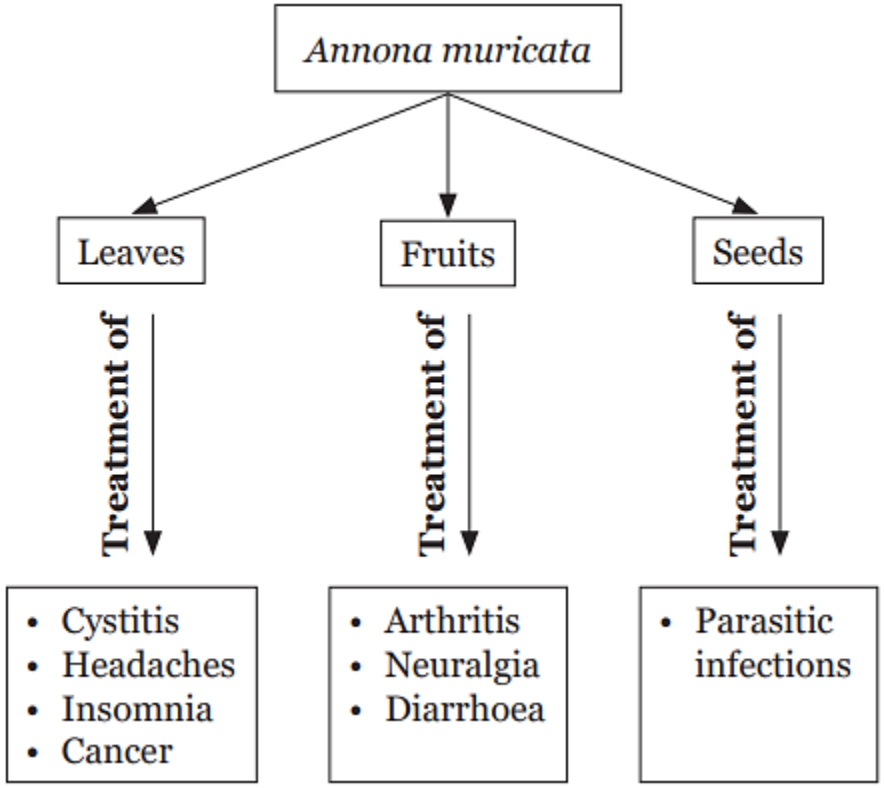
Shi B, Wang Z, Jin H, et al. Immunoregulary Cordyceps sinesis increases regulatory T cells to Th17 cell ratio and delays diabetes in NOD mice. ***Int Immunopharmacol***.2009 May;9(5):582-6.
Ji NF, Yao LS, Li Y, et al. Polysaccharide of Cordyceps sinesis Enhances Cisplatin Cytotoxicity in Non-Small Cell Lung Cancer H157 Cell Line. ***Integr Cancer Ther***.2011;10(4):359-67.
Cho HJ, Cho JY, Rhee MH, et al. Cordycepin (3'-deoxyadenosine) inhibits human platelet aggregation in a cyclic AMP-and cyclic GMP-dependent manner. ***Eur J Pharmacol***. 2007 Marr 8;558(1-3):43-51.


# Mangosteen

- Xanthones: Alpha-mangostin,  beta-mangostin
- Tannins
- Mangostinone
- Flavonoid: Epicatechin
- Aromatase inhibitory activity, inhibit COX-1 and COX-2 enzyme, Histamine and Serotonin receptor blockers and antioxidant effects
- In practical traditional Tai medicine, the pericarps of mangosteen were used to treat symptoms such as abdominal pain, leukorrhea, gonorrhea, and inflammation
- Current pharmacological research has revealed that the compounds isolated from the fruit hull exhibit antioxidant, anti-inflammatory, antinociceptive, antitumor, and anti-microbial effects.
- Among all secondary metabolites from mangosteen, xanthones were found to be one of the most effective antitumor components. May interact with anthracyclines, alkylating agents and platinum compounds.
- **Garcinone E (GE)** exerted similar and possibly enhanced anticancer properties in the tested cancer cell lines.
  - ***Induces apoptosis and inhibits migration and invasion in ovarian cancer cells***

Sci Rep. 2017 Sep 6;7(1):10718. doi: 10.1038/s41598-017-11417-4.
***J Ethnopharmacol*** 2017;198:302-12.

# Soursop (Annona muricata L.)




- The specific bioactive constituents responsible for the major anticancer, antioxidant, anti-inflammatory, antimicrobial, and other health benefits of graviola include different classes of annonaceous acetogenins (metabolites and products of the polyketide pathway), alkaloids, flavonoids, sterols, and others.

Yajid AI, Ab Rahman HS, Wong MPK, Wan Zain WZ. Potential benefits of Annona muricata in combating cancer: a review. Malays J Med Sci. 2018;25(1):5–15. https://doi.org/10.21315/mjms2018.25.1.2

# THANK YOU