Substrates for enteral and parenteral nutrition Topic 7

Module 7.1.

Substrates used for enteral nutrition: tube feeding

Aleksandra Kapala
Chemotherapy Daily Unit
Cancer Centre – Institute of Oncology,
Warsaw, 02-781, Poland

Ryszard Choruz
First Chair and Department of
General & GI Surgery,
Medical College Jagiellonian University
40 Kopernika St. 31-501 Krakow, Poland

Stanislaw Klek
General and Oncology Surgery Unit,
Stanley Dudrick's Memorial Hospital,
15 Tyniecka Str.,
32-050 Skawina, Poland

Learning objectives:

- To know the main components of commercially available enteral diets;
- To know the indications for oral nutritional supplements (ONS) and management of this nutritional support;
- To know the indications and benefits of various enteral formulas;
- To know how to choose the most appropriate formula for the patient.

Contents:

Key messages:

- Nutrients included in enteral formulas are sourced from natural products like cows' milk, soy, fish, olives and others;
- Commercially available enteral diets can be used in treating malnutrition, as well as in its prevention;
- Oral nutritional support should be recommended for all patients who are malnourished or at risk of malnutrition and who cannot cover their nutritional needs with normal, balanced diet. They must be able to swallow safely and nutrition via the GI tract must be possible;
- Oral nutritional supplements are foods for special medical purposes; the aim of ONS is to improve the patient's overall food intake in order to improve clinical outcomes;
- ONS have proven their effectiveness. Their use contributes to a decrease in mortality and postoperative complications, and increased body weight and quality of life (QoL);
- Standard tube diet is suitable for most patients and reflects the macro- and micro-nutrient requirements for the healthy population;
- Standard tube formulas can be modified, when specific clinical effects are needed;
- Disease-specific formulas are modified to create optimal conditions for treatment and to improve nutritional status in respect of those diseases.

1. Introduction

Humans need energy and nutrients in adequate amounts and proportions for proper growth and maintenance of health. Those requirements for most healthy people in the population are defined by nutrition standards in accordance with current states of knowledge. Compliance with guidelines based on these nutrition standards allows us to protect the population against the effects of deficiency and of excess nutrients. Knowledge of the nutrition standards helps us to plan the food supply and health-oriented educational programs at the macro scale, for example at the level of whole populations as well as in individual menus. The nutrition standards are used to assess the nutritional quality of food products on the market, the preparation of new products, including fortified and special purpose foods, and to develop standards for the nutritional labelling of products. Nutrition standards have some limitations: they are designed for specific population groups, specified in terms of gender, age, physiological state (eg. puberty, pregnancy) and level of physical activity. Therefore the individual needs of ill people may differ from those included in the nutrition standards. However, they should be the starting point for the preparation of special diets.

The first-developed nutrition standards met the needs in only 50% of the study population, and identified *de facto* the group average demand for nutrients, known today as the EAR (Estimated Average Requirement). Currently developed nutrition standards are covering the needs of 97.5% of the healthy population and are set at this level as the recommended daily intake or RDA - Recommended Dietary Allowances.

In the 80's Truswell suggested that nutrition standards should be determined at three levels:

— lowest: only for the nutrition assessment (DLL - Diagnostic Lower Level)
— average recommended intake (RDI - Recommended Dietary Intake)
— upper: the level above which adverse effects are expected (UL-Upper Level).

According to these findings, in 1992 the European Union accepted the following definitions: Lowest Threshold Intake (LTI), Population References Intake (PRI) and the Average Requirement (AR). In the U.S. and Canada the lowest level does not appear, but the concept of a group of estimated average requirements was adopted – EAR. The recommended intake (RDA) - Recommended Dietary Allowances is then EAR + 2 SD, and yields the concept of a sufficient intake or AI - Adequate Intake.

Most often encountered in practice are the EAR, the RDA, and the AI. The upper level of consumption (UL) is taking on special significance at present in the face of the mass fortification of food and uncontrolled or involuntary taking of dietary supplements (1-6).

Clinical nutrition, to treat malnutrition, comprises various nutritional interventions, including oral, enteral and parenteral nutrition.

Nutritional support in the oral form should normally be recommended to all patients who are unable to cover their daily energy requirements and other components of the diet. The following options are available to improve nutrient delivery:

- professional dietary advice;
- diet fortification with natural products;
- addition to the diet of complete and/or incomplete industrially produced diets - oral nutritional support (ONS) / sip feeding;
- enteral tube feeding

If the patient is unable to cover his/her nutrient demands with oral diet, tube feeding should be applied. It can be used in patients with a functioning gut, who are unable to meet their nutritional needs by oral feeding alone; it decreases complications and mortality. Appropriate choice of the site of feeding within the GI tract, where the formula is introduced, and the type of diet are crucial to achieve positive effects. A wide selection of commercially available enteral diets exists. The knowledge of substrates used to manufacture enteral diets is crucial to ensure the most appropriate nutritional treatment.

There is always a need to explain to the patient and/or his caregiver what kind of formula is planned and what it consists of.

During nutritional intervention, especially in the long-term, cooperation with the caregiver and patient is very important. They should receive complete information in

order to understand that the nutrients introduced through a tube to the GI tract are safe and suitable to meet nutritional needs.

2. General characteristics of enteral diets

Formula diets for enteral nutrition include those for oral feeding and those for tube administration. All of them are created according to the same regulation – European Commission Directive 1999/21/EC of 25 March 1999, and are called 'dietary foods for special medical purposes' (FSMPs) (7). This is a category of foods which are specially processed or formulated and which are intended for the dietary management of patients under medical supervision.
The wide selection of enteral diets allows us to choose the most appropriate formula for the patient. There are several types of products (8) that can be used during oral and/or tube feeding, e.g. standard energy and high energy; adult and paediatric; polymeric, oligomeric and monomeric; standard and disease-specific. The Directive of the European Commission guarantees that 1500 kcal of every nutritionally complete formula contains 100% of the recommended daily allowances for non-energy nutrients including all the key micronutrients. Commercially produced enteral diets are available in the form of powders and ready-to-use solutions.

3. Description of substrates used for enteral nutrition

The basic macronutrients used to produce ONS are extracted from natural foods.

3.1. Carbohydrates

The primary source of carbohydrate is generally a starch (typically maize) hydrolysed to oligosaccharides – maltodextrins - which are the main carbohydrate component of the nutrition mixture and reduce its osmolality relative to a glucose-based preparation. A small percentage of glucose (glucose syrup) is nonetheless usually present, which increases the osmolality. Fructose is rarely present in ONS, other than in some diabetic feeds. Lactose may be present in trace amounts, but most formulas do not contain lactose. Sucrose used as a sweetener, improves the flavour of ONS, and increases compliance, but also increases the osmolality of the solution.
Dietary fibre is a large group of substances which, except for lignins (polyphenols) are carbohydrates; it fulfils specific functions. Natural sources of fibre include fruits, vegetables, whole grains, legumes, potatoes, corn, and milk. In terms of chemical structure dietary fibre can be divided into: resistant starch (RS) (I-IV), inulin, oligosaccharides (alpha and non-alpha-glucans, rafinose, stachyose, verbascose, fructo- and galacto-oligosaccharides), non-starch-polysaccharides (NSP) (cellulose, hemicellulose, pectin, gums, mucilage). From the physiochemical point of view dietary fibre can offer many benefits which can be summarized as follows:
1. Water-soluble fibre: lower absorption of glucose and lipids, good substrates for fermentation by colonic bacteria – the end-products of this process are short-chain fatty acids (SCFAs) (mainly butyrate, propionate, and acetate). Butyrate is an important nutrient for colonic epithelium. Examples: pectins, gums, mucilages, fructo- and galacto-oligosaccharides, inulin;
2. Water-insoluble fibre: because of water-holding capacity increase bulk (stool mass) in large intestine, poor substrate for fermentation. Examples: lignin, cellulose, hemicellulose B;
3. Prebiotics: some types of fibre beneficially affect the host by selectively stimulating the growth and/or activity of bacterial species in the colon. Examples: inulin, fructo- and galacto-oligosaccharides. They support growth of beneficial species like lactobacilli and bifidobacteria, which can reduce the growth of potentially pathogenic species like Clostridium difficile.

3.2. Lipids

Lipids are present in the enteral diets mainly as triglycerides (SFA, MUFA PUFA) and phospholipids. Lipids used in the production of enteral diets are derived from natural plant oils: soybean, sunflower, corn, grapes, safflower and rapeseed oil; and from fish, in order to obtain the n-3 fatty acids. Coconut oil is a source of MCT. The detailed content of each lipid in each ONS depends on the intended clinical indications, and ranges from 0% (ProvideXtra, Nutridrink Juice Style, ENSURE Enlive, ENSURE Cleare) to 99% (Calogen).

3.3. Proteins

The protein sources used in enteral diets production are derived from animal and vegetable origins. The most commonly used are the casein and whey protein fractions of cow's milk. They contain all the essential amino acids and are characterized by a high degree of digestibility. Other animal proteins used to produce ONS include egg ovalbumin and gelatin (collagen hydrolysate). Vegetable proteins come mainly from soybeans and peas. Manufacturers often associate multiple protein sources in one supplement, usually casein and soy protein.

3.4. Omitted substances in enteral diets

One of the main advantages of enteral diets is the fact that they do not contain substances which could potentially provoke intolerance (lactose, gluten) or which could be present in usual diets in excess of what is safe for some patients (cholesterol, purine). Trace amounts of lactose <1g/100 ml are present in some of the ONS, because they are produced from powdered concentrates of highly concentrated (85%), milk proteins and may include a "contamination" of lactose. Gluten is not present in enteral diets because their manufacture does not use gluten-containing cereals, (wheat, barley, rye, oats), but gluten-free corn. For the production of these diets no animal fats are used, so they do not contain cholesterol, and because the main source of the protein is casein and soy, with no animal meat, they contain no purines. Therefore, enteral diets are safe for patients with (for example) glucose intolerance, coeliac disease, hypercholesterolaemia and gout.

3.5. Vitamins, minerals, trace elements

In order to comply with the EC Directive, the quantity of all complete enteral formulas that contains 1500 kcal must also contain the amount of vitamins, minerals and trace elements, which cover 100% of the RDA. For standard ONS this goal is usually achieved with a daily volume of 1000 ml.

3.6. Special ingredients

Special ingredients in the ONS have the status of functional components of the diet, because they potentially give certain health benefits through their impact on a variety of mechanisms, such as:

- improvement of immune function,
- inhibition of inflammatory processes,
- reduction of oxidative stress.

Those special components include:

1. Antioxidants: carotenoids with lutein and zeaxanthin, vitamins C and E, selenium. Their basic function is to reduce oxidative stress and the production of free radicals. It is worth noting that many of the antioxidants available in the normal diet are not found in ONS, eg lycopene in tomatoes, isoflavones in soybeans, polyphenols in grapes, allyl sulphides in onions, garlic and leeks, flavonoids in numerous fruits and vegetables;
2. Omega-3 fatty acids and PUFAs.

3. Nucleotides. They are the building blocks of DNA, RNA, ATP, cAMP, FAD, NAD and UDP-glucose. Nucleotides support the immune system, and may reduce the prevalence of infections and length of stay in hospital, especially in patients with GI cancer undergoing major elective surgery. Nucleotides are synthesized *de novo* from glutamine, glycine, aspartate, CO_2 and tetrahydrofolate, but during catabolic stress this may be not sufficient. Especially compromised are gut and gut-associated lymphoid tissue. Nucleotides influence the T-helper lymphocytes, macrophages and the expression of cytokines IL-2, IL-6, IL-8;
4. Glutamine. This non-essential amino acid plays a crucial role in the functions of the immune system, skeletal muscle and GI tract. It positively affects tissue repair and defends against oxidative stress (synthesis of glutathione), reduces GI bacterial translocation, activates lymphocytes, macrophages and expression of IL-1, IL-2, stimulates enterocyte proliferation and protects the GI mucosa;
5. Arginine. This non-essential amino acid stimulates proliferation of lymphocytes, enterocytes, and fibrocytes by stimulating the release of growth hormone. Conversion of arginine to cytrulline by NOS (nitric oxide synthase) produces nitric oxide (NO). NO in moderate amounts leads to anti-inflammatory effects but excessive production of NO has pro-inflammatory effects and increases GI vascular permeability. Arginine may be potentially harmful in patients with sepsis as it can increase the production of proinflammatory cytokines. A safer route may be from glutamine supplementation to increase the production of arginine from citrulline.
6. Micronutrients. Nutrients like vitamins: A, D, B6, B12, and folic acid, and trace elements like zinc, copper, iron, and manganese, can positively affect the skin/mucosa barrier, the function of lymphocytes and macrophages, and production of antibodies, cytokines, and prostaglandins. The evidence shows that only patients with burns generally require higher than normal doses of micronutrients.

4. Types of oral nutritional supplements

There are many supplements commercially available. They differ in composition, purpose and the form (liquid, semi-liquid or solid). ONS can be divided into:

4.1. Nutritionally incomplete oral supplements

Content: only protein (Protifar100% Whey Protein Powder, Soy Protein Powder), only carbohydrates (Fantomalt), carbohydrates and minerals (Preop, Polycose), only fats (Calogen), fat-free formulations containing other macro-and micronutrient supplements (ProvideXtra, Nutridrink Juice Style, ProMod, Ensure Cleare, Ensure Enlive, Glutamine Plus), supplements containing only vitamins and/or minerals in the form of pills, powders, drinks, etc. Nutritionally incomplete supplements can not be the only source of nutrition, and serve only to complement the normal, oral diet.

4.2. Nutritionally complete oral supplements

Contain all macro-and micronutrients in a balanced format with protein, fat, carbohydrate, vitamins and minerals. Nutritionally complete supplements can be divided between standard and special (for specific diseases). Standard formulas reflect the proportions of the ingredients of a normal oral diet, and under EU law must provide 100% of the RDA for vitamins and minerals in the quantity that supplies 1500kcal.
This is effective enough for most patients, but some clinical situations associated with increased requirements or loss of nutrients may require additional supplementation.

4.2.1. High-energy and high-protein ONS

In terms of energy and protein content ONS can be divided into standard, high-energy, and high-protein diets, and those that are high in protein and energy. These enhanced

types of ONS are recommended in patients who are malnourished or at high risk of malnutrition in order to cover the necessary total daily calorie intake and/or the increased protein demand in catabolic states. They may be useful in the perioperative period, during the diagnosis and treatment of various diseases, in recovery from acute illness, in the elderly, when elderly patients for various reasons, are not able to receive adequate amounts of nutrients. Representative nutritionally complete feeds are compared in **Table 1**.

Table 1. Typical complete, high-energy and high-protein ONS from some of the principal manufacturers.

Name	**Nutridrink Protein Compact**	**Hi-Cal**	**Resorce 2.0**	**Fresubin Protein Energy Drink**	**Nutricomp Drink Plus**
Producer	Nutricia	Abbott	Nestle	Fresenius Kabi	Braun
kcal/ml	2,4	2,0	2,0	1,5	1,5
Protein					
g/100ml **%**	14,4 24	8,35 16,7	9 18	10 27	6 16
Fats					
g/100ml **%**	9,4 35	8,9 40	8,7 39	6,7 40	5,0 30
Carbohydrates					
g/100ml **%**	24,4 41	21,6 43	21,4 43	12,4 33	20 54
Volume ml	125	237	200	200	200
Special ingredients	vit.C, E, selenium	vit.C, E, selenium	vit.C, E, selenium	vit.C, E, carotenoids, selenium	Omega-3 vit.C, E, selenium

In high-energy diets the increased caloric value results from removal of water and from the increased amount of fat (> 30%). The average content of lipids in the high energy ONS ranges from 30-45%. High energy ONS are nonetheless characterized by higher osmolality (mOsm/kg H_2O) and osmolarity (mOsm/L), which may cause osmotic diarrhoea and thus reduce compliance. In patients on high-energy diets additional water should anyway be given separately to the diet menu.

High protein diets contain 20-25% protein, and more than 4 grams of protein per 100 ml. They are designed for malnourished patients with coexisting inflammation and increased catabolism and/or loss of protein. In terms of content the nitrogen is usually presented in polymeric ONS format, containing whole protein molecules (eg: Nutridrink Protein, Promote, Ensure High Protein).

Oligomeric ONS-formulas comprising peptides consisting of 5-50 amino acids, and similarly short carbohydrate chains. They are designed for patients with malabsorption syndromes, such as from Crohn's disease, or radiation enteritis. They can also be useful if nutritional intervention is started after a long period of starvation. Examples of oligomeric diets are: Peptisorb, ProvideXtra, Optimental, Vital, Perative, Pivot.

Monomeric elemental ONS (based on glucose and individual amino acids) are dedicated to patients with rare, genetically determined metabolic diseases or severe food (protein) allergy; examples are presented in **Table 2.** They may provide a balanced content of all the (essential) amino acids or have a restricted profile for those with specific disorders.

Table 2. Examples of amino acid–modified feeds for genetic disorders

Amino acid-modified feed	Disorder	Characteristic
Cyklinex-2	urea cycle disorder, gyrate atrophy or HHH syndrome	non-essential amino acid-free
Glutarex-2	glutaric aciduria type I	lysine and tryptophan-free
Hominex-2	vitamin B6-nonresponsive homocystinuria or hypermethioninemia	methionine-free
I-Valex-2	disorder of leucine catabolism	leucine-free
Ketonex-2	maple syrup urine disease (MSUD)	isoleucine-, leucine- and valine-free
Phenex-2	phenylketonuria	phenylalanine-free
Propimex-2	propionic or methylmalonic academia	methionine- and valine-free; low in isoleucine and threonine
Tyrex-2	tyrosinemia types I, II, III	phenylalanine- and tyrosine-free

Sometimes polymeric high-protein formulas contain amino acid supplements of special importance for metabolism: glutamine, arginine, taurine, carnitine, CaHMB (calcium-ß-hydroxy-ß-methylbutyrate). HMB is a naturally occurring amino acid in human muscle and some plants. CaHMB is used to preserve or rebuild muscle mass in populations in whom loss of lean body mass (LBM) would increase risk of injury, disability, or mortality. After the 40th year of life approximately 8% of LBM is lost per decade of life even in the healthy, and after the 70th year this may rise to 15%. CaHMB could be effective in rebuilding LBM in the elderly as well as in persons with chronic diseases such as AIDS, pulmonary disease and cancer. ONS containing CaHMB exist (eg. Ensure Complete and Ensure Muscle Health, Juven also contains glutamine and arginine).
Before using high-protein ONS, it is important to be sure that the patient's renal function is satisfactory. High energy and high-protein diets have increased amounts of fat >30% and/or protein >20% and reduced water; this combination yields high osmolality which can cause osmotic diarrhoea and poor compliance (examples: Nutridrink Compact Protein, Protein Energy Drink Plus).

4.3. Supplements for specific diseases

They are designed for specific groups of patients with special nutritional requirements. The most commonly encountered in clinical practice are designed for: diabetes, renal failure, cancer, liver failure, disease of the pancreas and biliary tract, respiratory diseases, and to prepare the patient for surgery.

4.3.1. ONS for patients with diabetes

ONS for diabetes are similar to the standard diet. They can be isocaloric (Glucerna, Diasip) and hypercaloric (Diben, Glucerna 1.2 and 1.5 kcal/ml). Sucrose in these ONS is replaced by sweeteners including: acesulfame K, sodium saccharins, fructose. The formulations contain more polysaccharide, and the total carbohydrate content is typically 35% of the energy provision, characterized by a high content of soluble and insoluble dietary fibre (soya, tapioca), with an average of 6 types. Rapidly assimilable MUFA fats constitute as much as 35-55% of the energy, their high content helping to reduce

postprandial glucose, HbA1c and insulin requirements. LFA are reduced to <25%. Comparison of some typical ONS for diabetics are presented **in Table 3.**

Table 3. ONS for diabetics

Name and producer	Diben Drink Fresenius Kabi	Diasip Nutricia	Glucerna Abbott	Standard
Kcal/ml	1.5	1	1	1 – 1.5
Protein				
g/100ml	7.5	4.0	4.1	4.0
%	20	16	16.7	16
Fats				
g/100ml	7.0	5.4	5.4	1.7
%	42	48.7	49	
SFA	1.7	0.6	-	
MUFA	3.8	3.8	1.9	
PUFA	1.5	1.0	-	1.0
Carbohydrates				
g/100ml	13.1	8.8	9.5	17.6
%	35	35.3	34	
Fibre				
g/100ml	2.0	2.5	1.44	0-2.0
Special ingredients	MCT, ALA, EPA +DHA Carotenoids	Carotenoids	ALA, EPA+DHA taurine L-carnitine m-inosytol, carotenoids	none

4.3.2. ONS for patients with chronic renal failure (CRF)

There are two types of formulas for chronic renal failure: those for patients in the pre-dialysis period, and those for patients on dialysis. These are all calorie dense with 1.3-2 kcal/ml. ONS for patients before dialysis have a reduced protein content, down to 6-10% of energy sources, (ie 2-5g/100ml).
The main sources of energy are fats and carbohydrates, both at about 45%. The protein has a high biological value, and contains all the essential amino acids. Part of the fat provision is generally as MCT. The mineral content, which may contribute to the progression of renal failure (eg Na, K, Cl, Ca, P, Mg) is limited. Additionally these feeds contain carotenoids, L-carnitine, and taurine. Examples of ONS for predialysis patients include: Survimed renal, Renilon 4.0, Suplena; on dialysis: Renilon 7.5, Nephro.
Formulas for patients on dialysis have a protein content of 15-18%, or 7.5-8.1 g/100mL. The remaining energy is derived from carbohydrate and fat, again relatively equally distributed at 40-45% each. In dialysis patients electrolyte disturbances (especially potassium and phosphates) will be closely monitored and are often more readily aligned by the intravenous route.
Ketosteril® is a special kind of ONS for CRF. It contains five essential amino acids and another five amino acids in the form of their hydroxy and keto analogues as calcium salts, that are: alpha-ketoleucine, alpha-ketoisoleucine, alpha-ketovaline, alpha-ketophenylalanine and alpha-hydroxymethionine and is suitable for use in patients with GFR <25ml/min, to supplement very low- protein diets (<40g of protein per day). These are the "carbon skeletons" of essential amino acids. In the process of transamination

nitrogen from non-essential amino acids is attached to them yielding the amino acids needed. Ketosteril is produced in tablet form (usual dose 4-8 tablets per day).

4.3.3. ONS for oncological patients

ONS for oncological patients are mostly high in both energy and protein, to help to address anorexia and tumour-related catabolism; they are presented in low volumes (eg 125-150ml per portion). They contain one or more additional components, such as antioxidants, including carotenoids and selenium, the omega-3 fatty acids, EPA and DHA, or MCT, prebiotics, and fibre. Examples include: Forticare, Supportan, Nutridrink Protein Compact, Fresubin Protein Energy Drink, Drink Nutricomp Plus, Ensure Plus, Ensure Complete.

4.3.4. Immune modulating formulas

Formulas of this type contain special additives (such as omega-3 fatty acids, glutamine, arginine, nucleotides, BCAAs, antioxidants, high-protein, high-energy) in supraphysiological doses, with the intention of improving the immune response to metabolic stresses such as: trauma, infections, burns, surgery, radio- or chemotherapy. They are used primarily as enteral tube feeds in line with the recommendations of ESPEN, peri-operatively for patients with head and neck or upper GI tract cancer, and for those having major abdominal surgery, and after severe trauma. Immune modulating formulas are contraindicated in severe sepsis (increased mortality). Oral immune modulating supplements may be used if the patient does not need or agree to intubation. Immune modulating ONS are used in the course of infection and treatment of pressure sores - but there is no conclusive evidence about their effectiveness for these conditions. Many preclinical studies suggest a strong and beneficial immunomodulating effect of the additional components, but meta-analysis cannot confirm overall health gain. The effects are almost inevitably evaluable only for the proprietary combination of the components, and conclusions are therefore necessarily product specific. Examples of immune modulating ONS include: Cubitan, Perative, Pivot, Glutamine Plus, Juven, Oxepa.

4.3.5. ONS for liver disease

There is relative deficiency of the branched chain amino acids (BCAA: valine, leucine and isoleucine) in acute and chronic liver disease, which has been associated with a poorer prognosis and with encephalopathy. Supplements created for patients with liver disease therefore contain 2-3 times more BCAA and fewer aromatic amino acids which are the substrate for the production of toxins which increase encephalopathy. The overall content of protein is normal (average of 12% of energy from protein), there is normally no fibre, and the energy density is typically 1.3 kcal/ml. These formulas also contain 6-10-times more MCT, which helps to reduce the absorption of LCT and perhaps also cholestasis.
ESPEN recommends (Grade A) the use of BCAA in decompensated cirrhosis, alcoholic steatohepatitis and in some peri-operative liver transplant patients. Examples include: Drink Fresubin Hepa, Hepa Nutricomp.

4.3.6. ONS for pancreatic and biliary tract diseases

These are generally incomplete ONS, which contain a whole or pre-digested protein source (whey protein or hydrolysate or short peptides from peas), the carbohydrate source is mainly maltodextrin. They are fibre- and fat-free, with an energy content of 0.6-1.5 kcal/ml. They are proposed for: chronic pancreatitis, and cholelithiasis (gallbladder and biliary tract), but also in the case of some types of malabsorption in the course of: short bowel, Crohn's disease, chemotherapy and/or radiotherapy. Examples include: ProvideXtra, Nutridrink Juice Style, ENSURE Enlive, ENSURE Cleare.

4.3.7. ONS for respiratory system disorders

PULMOCARE is a high-calorie, low-carbohydrate formula designed to help reduce carbon dioxide production (by driving the respiratory quotient downwards), which may be helpful for patients with chronic obstructive pulmonary disease (COPD), cystic fibrosis, or respiratory failure. Some 55% of its energy content is derived from fat, of which 20% is MCT. Carbohydrates cover only 28% of the calories. Pulmocare is proposed for use in stable patients with chronic illness only as a supplement (300-600kcal extra/day), so that the majority of the CO_2 is produced from normal foods. Its potential positive effects are more likely to be realized by an overall improvement of nutritional status than a specific effect of the intended nutriceutical treatment with Pulmocare. In acute respiratory diseases it is reasonable to extrapolate from the good results in other conditions and to enrich the diet with omega-3 and antioxidants supplements, but there are no secure positive data for this.

4.3.8. Preparing the patient for surgery

In the immediate pre-operative phase (from 6 hours to 2 hours before the surgery) it is now recommended that patients are nourished actively. It has become conventional to provide 100% of the energy as a carbohydrate drink with additional electrolytes. The drinks have a low calorific value (0.5 kcal/ml) and a low osmolality, and are without fibre. The administration of carbohydrate drink is part of the ERAS procedure (Enhanced Recovery After Surgery). This practice reduces the feeling of hunger, thirst, nausea and anxiety before surgery, is safe, reduces insulin resistance and catabolism after surgery, and improves mood and reduces length of hospital stay. Suitable formulas are most effective if commenced 18 or more hours before the surgery, with a typical final 800ml on the evening before surgery and 400ml in the morning of the day itself.

5. General characteristic of enteral diets

5.1. Adults:

- 15-20% of energy from proteins
- 25-40% of energy from lipids
- 40-60% of energy from carbohydrates
- ˜1kcal/1ml
- ˜85% Water

5.2. Children:

- 10-15% of energy from proteins
- 30-50% of energy from lipids
- 50-60% of energy from carbohydrates
- Proportion of energy from proteins, lipids and carbohydrates depends on the age of the child
- ˜80-90% Water
- 0,65-1 kcal/1ml

5.3. Polymeric formulas

Polymeric formulas are usually nutritionally complete diets, mostly comprising intact macronutrients, and are suitable for patients with a functioning digestive system. Their composition reflects the reference values for macro- and micronutrients in the population. The common feature of this group of diets is the use of whole proteins as the

nitrogen source. Osmolality is close to physiological – 200-350 mosmol/kg. They are indicated for about 90% of enterally fed patients.
ESPEN guidelines (8-17) recommend the use of standard diets if only enteral nutrition is possible or eating has not proved feasible and the tolerance of that enteral feeding is good. Therefore those diets can be administered as first choice diets to the following groups of patients, if there are no contraindications, e.g. in ICU, surgery, oncology, Crohn's disease, acute pancreatitis, liver cirrhosis and alcoholic steatohepatitis, acute and chronic renal failure renal failure and haemodialysis, HIV, chronic heart failure, and neurological diseases (mainly stroke and motor neurone diseases). When disease-specific clinical effects are needed, the polymeric formulas can be modified, as shown in the diagram.

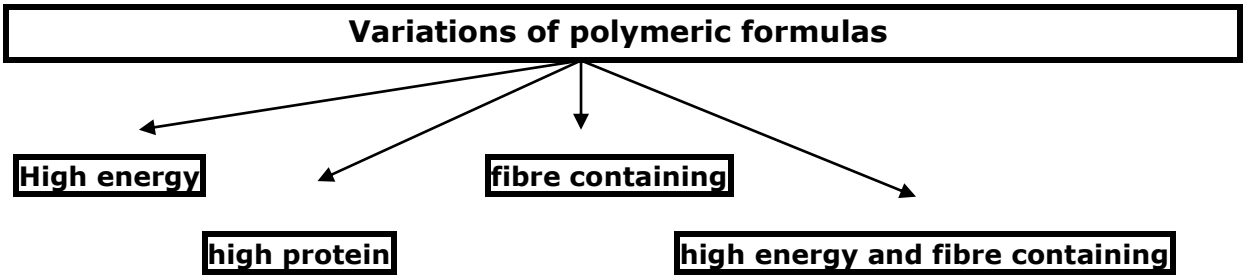

Fig. 1. Variations of polymeric formulas**.**

5.4. High energy formulas

Energy dense formula contains more than 1.2 kcal/ml and, as a general rule, contain less water (70-77%) than standard diets; the higher energy feeds with 2 or more kilocalories per millilitre additionally have an increased lipid fraction. Indications for the use of these diets include the need for fluid restriction, such as in cardiac and renal disease or decreased nutritional volume load. As the osmolality of high energy diets is higher, their tolerance may be worse and result in osmotic diarrhoea. Due to their higher lipid concentration high energy diets may also be suitable for patients with pulmonary disorders and in Cystic Fibrosis.

5.5. High protein formulas

High protein formulas are mainly used for patients in catabolic states, with severe malnutrition and problems with wound healing e.g. Crohn's disease, patients on haemodialysis or HIV infection. They contain 20% or more of total energy from protein.
NOTE: Higher protein and/or energy intake can be ensured by increasing the volume of formula regardless of their proportions.

5.6. Fibre-containing formulas

Historically, standard formulas were fibre-free. However the many advantages associated with dietary fibre have led to a change in philosophy such that in most of the world the inclusion of fibre has become the new default for formula feeding also. Fibre-free feeds remain available of course.
Fibre comprises carbohydrates which reach the colon undigested and are metabolically and energetically available there. The main components of dietary fibre are (according to

chemical structure): non–starch polysaccharides, inulin and oligosaccharides, resistant starch and lignin (18,19). They are components of plant cell walls and plant cells.

Table 4. Classification and sources of dietary fibre.

Dietary fibre	**Specific fibre**	**Sources**
Non–starch polysaccharides	Cellulose, hemicellulose, pectin, gums, mucilage	Whole-wheat flour, bran, vegetables, whole grain, apples, citrus fruits, oats, guar, barley
Lignin		Mature vegetables, edible seeds
Oligosaccharides	⟨–glucans, non-α-glucans, raffinose, stachyose, verbascose, fructo-oligosaccharides, galacto-oligosaccharides	Vegetables, onions, chicory, artichoke, banana
Inulin		Onions, artichokes
Resistant starch		Potatoes, maize

Solubility in water, fermentability, water – holding capacity and viscosity are major physicochemical features of fibre. There are also some specific fibres, mainly inulin, fructo – and galacto-oligosaccharides, with prebiotic properties.
Soluble fibres have effects on the absorption of glucose and lipids in the small bowel. They are usually good substrates for fermentation by colonic bacteria, which leads to the development of short chain fatty acids (SCFAs - butyrate, propionate, acetate) and gases (hydrogen, methane) (20). They have beneficial effect on the glucose absorption rate (21,22). The main food sources are: oats, barley, soy beans and citrus fruits. Functions of SCFAs include:

- Energy source for colonic mucosa
- Increase in absorption of sodium and chlorate as well as water
- Increase in proliferation of mucosal cells
- Increase in blood flow in mucosa
- Increase in mucus production
- Maintain the integrity of the mucosa

Insoluble fibres need to reach the large bowel to affect intestinal function. They retain more water than soluble fibres. They are usually a worse subject for fermentation and serve mainly to increase bulk in the large intestine. The food sources are mainly whole wheat and vegetables.
In practice, the distinction between soluble and insoluble fibres is difficult. Some of the insoluble fibres are also fermented, and not all of the soluble fibres have influence on glucose absorption (22).
Physiological effects of fibres (23):

- Slow gastric emptying and decrease appetite (helpful in body weight control)
- Viscous fibres can lower the plasma level of LDL and cholesterol; and reduce postprandial blood glucose and insulin responses (helpful in cardiovascular diseases and diabetes)
- Non-fermentable fibres have effects on faecal bulking and shortening colonic transit (prevention in constipation, diverticulosis, perhaps also colorectal cancer)

5.7. Oligomeric formulas (also called peptide feeds)

Oligomeric diets contain oligopeptides, mainly di- and tripeptides, instead of whole proteins, carbohydrates also as smaller molecules, and a higher percentage of MCTs as lipid source, which improves digestion and absorption. Their osmolality is, however, higher (300-600mOsmol/L), thus they cause osmotic diarrhoea more often than polymeric diets. There are no absolute indications.
Indications (24):

- Intolerance of polymeric diets in patients with a functioning GI system (Note: if intolerance due to milk protein allergy is present, use of a polymeric diet based on soya proteins may be possible)
- Impaired absorptive capacity
- After prolonged starvation
- Jejunal feeding (critical care patients, severe acute pancreatitis)
- Selected patients with short bowel syndrome
- Patients with Crohn's disease related fistulae
- Wasting in HIV patients with diarrhoea

5.8. Monomeric formulas (also called elemental feeds)

Monomeric formulas contain free amino acids as their source of nitrogen. Their osmolality is the highest (500-900). Severe malabsorption, and severe, multiple food allergies are the main indications. They will be tried in patients who prove intolerant of polymeric and oligomeric feeds.
Practical note: To avoid intolerance of oligomeric and monomeric diets caused by their higher osmolality, these formulas can be temporarily be diluted at the beginning of their administration, with e.g. 0.9% NaCl or 5% glucose.

5.9. Disease – specific formulas

Some diseases require special nutritional handling. These diets are designed to control the disease better and to decrease complications (14). However their benefits are mostly not proven. Usually they are more expensive and, if used inappropriately, may result in complications. There are many types of disease-specific formulas, some of them are described below.

5.10. Diabetes formulas

There are two types of diabetes formula available:
Classic – are very similar to standard formulas with fibre. They contain a higher proportion of polysaccharides, and sometimes sucrose is replaced with fructose. The fibre can modulate response to glucose by delaying gastric empting and bowel transit, reduction of glucose diffusion through unstirred water layer and reduced accessibility of α-amylase. Absorption of carbohydrates can be prolonged by increasing GLP-1 (glucagon-like peptide 1). Some kinds of fibre can also increase insulin sensitivity and improve diabetic control.
Modern (or MUFA) formulas – have been adjusted such that a proportion of the standard carbohydrate content has been replaced by mono-unsaturated fatty acids (MUFAs). MUFAs can cover up to 35% of energy. In these formulas fibre is also added. Data show that these diets reduce the postprandial rise of glucose concentration and enable more precise glucose control than standard formulas (25). In some studies the use of high MUFA diabetes formulas induced lower mean, fasting and postprandial glucose levels, and reduced insulin intake (18).
The putative clinical benefits of diabetes formulas remain unproven due to the lack of long- term studies.

5.11. Liver formulas

Enteral diets designed for use in patients with liver failure and hepatic encephalopathy are characterized mainly by their higher proportion of branched-chain amino acids (BCAAs): valine, leucine, isoleucine; and reduced amounts of the aromatic amino acids (AAAs) and of methionine. Usually these are whole protein diets with a higher proportion of MCTs in their lipid fraction to reduce the presumed problems with absorption in cholestasis.
In many patients with hepatic failure, ascites can be seen. In these states fluid restrictions are needed; therefore most hepatic diets have high energy and low sodium. According to the ESPEN guidelines for liver disease nutrition these formulas are indicated in patients with encephalopathy, in alcoholic steatohepatitis, decompensated cirrhosis and in some postoperative patients (15).

5.12. Renal formulas

There are several types of formula used in patients with renal failure (15):
- Standard formulas – suitable for many patients with mild to moderate renal impairment
- Renal formulas, Renal specific infant formulas - generally protein restricted, but enriched in essential amino acids and ketoanalogues, with reduced electrolyte content to minimize blood urea nitrogen and reduce accumulation of toxic products. These are intended for patients with renal impairment in whom a low protein oral diet would otherwise be prescribed.
- "Dialytic formulas" – high protein content (oligopeptides and free amino acids), but reduced amount of potassium and phosphate; high energy (1,5-2 kcal/ml), variably supplemented with histidine, taurine, tyrosine and carnitine. These are high protein diets intended for patients already established on dialysis (haemodialysis or peritoneal) in whom nitrogen losses are high.

The choice of diet depends on stage of illness and the type of treatment(15).

	Type of formula
Acute renal failure	Standard formula is adequate for the majority of patients; In the case of electrolyte derangements a specific renal formula can be advantageous
Conservatively treated chronic renal failure (CRF)	Standard formula only for short-term feeding For EN > 5 days use special renal formula Essential amino acids and ketoanalogues in association with very low protein formulas – to preserve renal function
CRF during haemodialysis	Dialytic formulas
CRF during peritoneal dialysis therapy	(Data almost exclusively from paediatric patients) EN via tube should be considered in all children, but particularly in infants and children under 5. Renal specific infant formulas or standard paediatric formulas

5.13. Pulmonary formulas

Patients with pulmonary insufficiency retain CO_2 and experience O_2 depletion. Standard formulas, in which the energy stems mostly from carbohydrates, induce somewhat greater respiratory demand, as the O_2 consumption is responsible for proportionally greater CO_2 production because the respiratory quotient is higher than on high fat diets.

Therefore enteral diets designed for patients with respiratory diseases contain a higher proportion of energy from fat, which results in a lower formation of carbon dioxide. Results of clinical studies, are, however, confusing and do not always support the use of these diets, even in patients with advanced COPD.

5.14. Immune modulating formulas

Formulas, which contain glutamine, arginine, ω3-fatty acids, nucleotides and antioxidants, individually or in combination, are designed to affect the inflammatory response. They are indicated in the following contexts (9):

- Major surgery for abdominal and oesophageal cancer
- Major head and neck surgery for cancer
- Mild sepsis (APACHE II < 15)
- Severe trauma
- Malnourished patients undergoing major abdominal surgery
- ARDS

Detailed description of immunodiets is presented in another module, but it should be noted that there is a good evidence base for their use as outlined above, its understanding hampered by the fact that as the preparations are mixtures it remains unclear which component(s) is(are) most important.

5.15. Ketogenic formulas

A ketogenic diet is a strict diet, which consists of minimal amounts of carbohydrate and protein and increased amounts of fat (26). Ketogenic diets therefore create conditions which simulate the body's response to starvation, where fat is the primary source of energy. They can be beneficial due to the fact that in a fasting state amino acids cannot provide sufficient energy for the brain, and that the liver produces ketone bodies from the fatty acids. The ketogenic diet is also well established as an alternative therapy for intractable epilepsy (27), but the exact mechanism by which ketosis reduces the frequency and severity of seizure episodes is unknown and needs further investigation. In ketogenic diets the fat : non-fat (carbohydrates and proteins) ratio is typically 4:1 (by weight).

The expanding use of ketogenic diet includes the following indications (28):

- Epilepsy
  - Intractable epilepsy
  - Super-refractory status epilepticus
  - Dravet syndrome
  - Myoclonic astatic epilepsy
- Metabolic disorders
  - Glucose transporter type 1 deficiency
  - Pyruvate dehydrogenase complex deficiency
  - Phosphofructokinase deficiency
  - McArdle disease
- Neurologic disorders
  - Alzheimer's disease
  - Parkinson's disease
  - Amyotrophic lateral sclerosis
  - Traumatic brain injury
  - Autism
  - Depression
  - Migraine

5.16. Metabolic disease-specific formulas

There is a great variety of enteral diets specially prepared for different metabolic diseases. Some of them are nutritionally complete, but restricted, for example diets used in phenyloketonuria or galactosaemia; some of them are just food fortifiers, which can be added to standard diets (e.g. the agent used in Smith-Lemli-Opitz-Syndrome treatment). Indications for the use of these individual formulas are usually limited to specific clinical conditions. [29]

6. Summary

The first step in proper nutritional intervention is the assessment of nutritional status. In the case of a diagnosis of malnutrition and/or high risk for its development, dietary counselling, food fortification and prescribing of ONS should be considered. When the nutritional goals cannot be met by this kind of treatment, artificial nutrition should be considered. ONS are indicated for all patients who are malnourished or are at high risk of malnutrition, can swallow safely and in whom oral feeding is possible. Equally, ONS should be stopped when the patient is re-established on adequate oral intake from normal diet. There are many ONS commercially available and the choice of formula depends on the nature of the disease/disorder. Oral supplements usually support a normal, balanced diet. Dysphagic patients with incomplete obstruction and a safe airway require a change in the texture/consistency of their diet and the volume and frequency of meals. ONS have proven their effectiveness.
In the case of enteral tube feeding, which should be used if the nutritional needs cannot be met with oral diet (including oral supplements), polymeric formulas and their variations are suitable for most patients with functioning digestive system and are generally well tolerated. In cases of food allergy, intolerance or absorption disorders, oligomeric or monomeric diets might be necessary. Disease specific formulas, used according to relatively strict indications, are intended to create optimal nutritional conditions for disease treatment. The great variety of commercially available enteral diets dedicated for tube feeding, presents the opportunity for highly individual selection to serve the patient and his disease, but the evidence base in favour of specific strageties is often lacking.

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