

UNIVERSITY OF PAVIA - ITALY  
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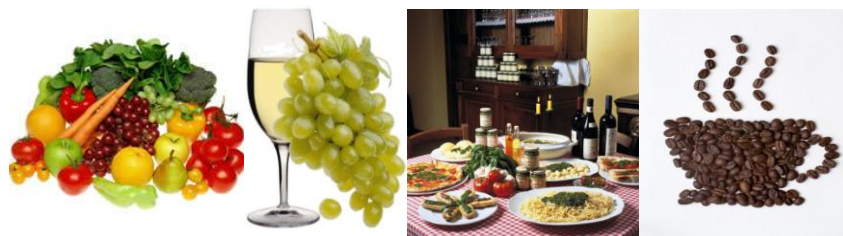
Bachelor in Dietetics

Director:

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# GUIDELINES FOR PATIENTS WITH HYPERHOMOCYSTEINEMIA

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### What is homocysteine?

Homocysteine is a sulphured amino acid that is generated by our organism from methionine, an essential amino acid that is in turn introduced in the human body by means of nutrition through a regular consumption of meat, eggs, milk and legumes.

Homocysteine's metabolism is regulated thanks to the specific action of specific enzymes and vitamins that are present in human blood. Particular reference is made to vitamins B6 and B12 and to folic acid.

If the intake of these vitamins is insufficient, Homocysteine accumulates in the bloodstream, causing damage to the walls of the blood vessels and modifying their structure and functionality.

Recent studies have proven that elevated plasmatic concentrations of Homocysteine are:

- connected to an increase of the risk of heart disease
- a risk factor for neuro-degenerative pathologies such as dementia and Alzheimer's
- present in pregnant women affected by pre-eclampsia, fetal growth defects, premature detachment of the placenta and spontaneous and repeated miscarriages
- an alarm signal for bone fragility. In a recent study, researchers have found that elevated levels of plasmatic homocysteine are an important and independent risk factor for osteoporotic fractures both in elderly men and women.

### Homocysteine: Plasmatic Values

HOMOCYSTEINE	PLASMATIC VALUES
NORMAL VALUE	5-9 $\mu\text{mol/L}$
<b>hyperhomocysteinemia</b>	
BORDERLINE	10-12 $\mu\text{mol/L}$
MODERATE	13-30 $\mu\text{mol/L}$
INTERMEDIATE	31-100 $\mu\text{mol/L}$
SEVERE	>100 $\mu\text{mol/L}$

Table 1 - Homocysteine plasmatic values

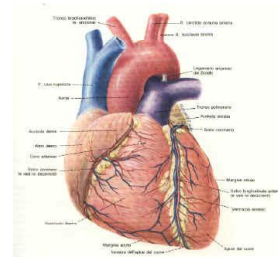
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## Who should undergo check-ups?

1. Those who have cardio-vascular risk factors

- Heart attack
- Thrombosis
- Re-vascularization
- Heart transplant



2. Pregnancy



3. Oral contraceptive therapy



4. Menopause

5. Osteoporosis



6. Unbalanced diet



## The causes of Hyperhomocysteinemia

The factors that may cause Hyperhomocysteinemia are:

- Genetic factors
- Nutritional factors
- Kidney-related pathologies
- Other pathological conditions

It is important to make sure that the plasmatic levels of homocysteine remain in the “normal range” because Hyperhomocysteinemia seems to:

- Favor atherosclerosis
- Make oxidative stress worse

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- Reduce vasodilatation
- Increase the activation, adhesion and aggregation of blood platelets, making way for the risk of thrombosis

### Prevention and cures

A strong correlation has been observed between the lack of certain vitamins (such as Vitamins B6, B12, and folic acid) and the plasmatic values of homocysteine. Therefore, it is important to pay attention to the daily assumption of these micro-nutriments with a varied and balanced diet.

### Therapeutic strategies

Where necessary, all patients in the following categories should pay particular attention to changes in their lifestyles:

- Patients with borderline Hyperhomocysteinemia (10-12  $\mu\text{mol/L}$ )
- Patients that require treatment with supplementary vitamins

The aim is to reduce the plasmatic values of homocysteine and subsequently modify the connected risk factors and clinical conditions.

By “changes in lifestyle” we mean the following:

- Increase in the intake of fruits and vegetables
- Elimination of smoke
- Increase in physical activities
- Reduction of alcohol use
- Reduction of caffeine intake

### Changes in lifestyle

Hyperhomocysteinemia is caused by a group of factors: some of these may not be changed (genetic factors, gender, age), others are difficult to change (pathological conditions, pharmacological therapies), but the factors related to certain lifestyles are fully modifiable (tobacco

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dependency, caffeine and alcohol abuse, wrong eating habits, low physical activity rates).

This means that a reduction in the caffeine and alcohol intake, a varied diet and a targeted vitamin intake (B6, B12 and folates), along with a non-smoking attitude can reduce the level of homocysteine even while the other causes may persist.

### Elimination of the habit of smoking

It is known that smoke increases arterial pressure and cardiac frequency and that these effects last well over the fifteen minutes which are necessary to smoke a cigarette.



Recent studies show that inflammation and Hyperhomocysteinemia can be important means by which smoke can cause atherosclerosis. One should also remember that, by interfering with metabolism of the folates, smoke inhibits their absorption. Studies show that some micro-nutrients in fruits and vegetables can have a preventive function. For this reason it is necessary to get used to consuming 5 or 6 daily portions of fruit and vegetables as is suggested in the INRAN (National Institute for Nutritional Research) guidelines for a healthy diet.

### Alcoholic beverages

Chronic alcohol abuse can cause damage to various systems:

- Central and peripheral nervous systems
- Digestive organs
- Cardio-vascular system
- Neoplasia
- Nutritional lacks of balance that may evolve into a state of malnutrition



A number of studies have shown the existence of a direct link between the plasmatic increase of homocysteine and the consumption of alcohol. Patients with moderate, intermediate and severe levels of homocysteine should avoid alcohol consumption.

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### Physical exercise

Sedentariness, meant as a lack of physical exercise, is a strong signal of future cardiovascular pathologies. Some studies have proven that aerobic physical exercise has positive effects on people with Hyperhomocysteinemia.



Therefore it is advisable for people with Hyperhomocysteinemia (from borderline to severe levels) to move, possibly every day.

For example, these people should go for a daily walk, they should go on bike rides, they should run or go swimming.

### Coffee



It is important to avoid or limit the intake of coffee. The reason for this is that some studies show that elevated concentrations of caffeine can interfere with the absorption of B group vitamins and this proves that there is a direct link between coffee consumption and the increase of homocysteine in blood.

### Change your diet often

It's good to always remember that no food is complete or perfect and that no food contains all the nourishing factors our body needs in the right quantity or proportions in order to satisfy our nutritional needs.



As a consequence, the easiest way to ensure a correct intake of all the necessary nutritional elements is to vary our nutriment choices often by following a varied diet.

Behaving this way means avoiding possible lacks of balance in nutrition and subsequent metabolic lacks of balance. It also means satisfying taste and fighting against the monotony of flavors. Diversifying our dietary choices means favoring our well-being and favoring a complete intake of vitamins and minerals and these have a regulating and protective function

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for the human body. In order to have a complete and balanced diet, each food group (as shown in tables 7-9) must be re-created following the indicated proportions and varying the food choices as much as possible.

### More vitamins B group



It has been demonstrated that the introduction of vitamins B group (more specifically vitamins B2, B12 and folic acid) in our bodies significantly reduces the plasmatic value of homocysteine, bringing it back to the suggested reference values.

### Characteristics of the vitamins B group

- vitamins B are molecules that cannot be synthesized by our body on its own, therefore they need to be introduced in our organism with our diet. These vitamins can be found in **fish, meat, fruits, vegetables, eggs and in dairy products**
- These vitamins are water-soluble and are eliminated through our urinary tract. Our body needs to assume a certain quantity of grams (g) or of micrograms ( $\mu\text{g}$ ) of these vitamins daily.
- When foods are cooked, these vitamins lose their specific characteristics. This is why we suggest to consume raw foods whenever it is possible, or to consume foods that are cooked at low temperatures and/or for a very short time (for example, we suggest steam-cooking), see table 2.

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### Cooking techniques and nutritional modifications






Cooking technique	Temperature	Hygiene issues	Nutritional aspects
Boiling 	100 (120 <sup>1</sup> )C	All pathogenic bacteria are destroyed. Spores and toxins are not destroyed <sup>2</sup> .	In vegetables, partial loss of minerals in the cooking liquid. Foods may be dressed when raw.
Steam cooking 	<100° C	All pathogenic bacteria are destroyed. Spores and toxins are not destroyed.	Lower loss of minerals and vitamins compared to boiling. Foods may be dressed when raw.
Traditional oven cooking 	180-220° C	Rapid superficial sterilization with destruction of all pathogenic bacteria and spores. Inactivation of all bacterial toxins <sup>3</sup> .	A smaller quantity of fats may be used.
Grilling 	>200° C	Rapid superficial sterilization with destruction of all pathogenic bacteria and spores. Inactivation of all bacterial toxins.	If the superficial parts of the foods are burnt, cancer agents may incur. Dressing fats may be eliminated.
Frying 	>180-190° C	Rapid superficial sterilization with destruction of all pathogenic bacteria and spores. Inactivation of all bacterial toxins.	The products absorbs a lot of oil and is therefore very rich in fats. In high temperatures, the oil degrades itself and may develop harmful substances <sup>4</sup> .

Table 2 - Cooking methods

<sup>1</sup> In pressure cookers

<sup>2</sup> For recipes that contain eggs, meat and fish, in case of boiling, the boiling of the cooking water should be less than 10 minutes; in case of steam cooking, foods need to be exposed to the steam for a longer period of time, based on the dimensions and on the type of product

<sup>3</sup> If the cooking time is not sufficient for the dimensions of the product, some parts of the product may not be fully cooked, therefore some parts may not be fully restored

<sup>4</sup> is important to not use frying oil twice



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- Highly conservable foods, or poorly preserved foods may lose their nutritional characteristics and their vitamins B. It is therefore better to consume fresh fruits and vegetables.
- It is better to choose not only processed foods because the procedures which these foods are undergo may deprive them of nutritional elements.
- In order for the assumption of vitamins B to be efficient, a good rule is for foods rich in Vitamins B, to be included in every meal of the day (thus meaning in the 3 main meals of the day and in 2 snacks), based on what is suggested for a correct diet. Excessive use of alcohol, coffee, sugar, tea and cigarettes must be avoided because they reduce the absorption of vitamins B significantly.

### Deficiency of vitamins B

Which symptoms warn us of a possible vitamins B deficiency? We may notice grumpiness, fatigue, difficulty in concentrating, memory loss, mood swings, leg cramps, loss of appetite and bowel issues. We must also pay specific attention to our nails and hair: if they seem fragile for extensive periods of time and if they appear dehydrated, this may be a signal of a lack in vitamins levels.

### Foods rich in vitamins B

Whenever there is a lack in vitamins B or whenever there is plasmatic hypercysteinemia, it is very important to assume foods rich in this vitamins. It is therefore important to know where folacin, B6, and B12 vitamins may be found (tables 3, 4 and 5).

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**FOLIC ACID (Vitamin B9 or folacin):** it can be found mainly in dark green vegetables.

A **200µg per day** intake is recommended.

Concentrations	Vegetables and legumes	Fruit	Cereals	Eggs and cheese
High concentration of folates (300-100 µg/100g)	Asparagus, broccoli, artichokes, cabbage, dried beads, Brussels sprouts		Breakfast cereals	
Medium high concentration of folates (99-40 µg/100g)	Spinach, beets, lettuce, cherry tomatoes, indivia, cauliflower, beans, broad beans	Oranges, mandarins, kiwi, avocado, dried fruits (almonds, nuts, pistachios)	Tomato pizza	Eggs, cheese (parmesan, camembert, blue cheese, taleggio cheese)
Medium concentration of folates (39-20 µg/100g)	Potatoes, tomatoes, chicory salad, carrots, peppers, dried peas	Grapefruit, strawberries	Whole wheat bread, bran pasta, crackers	Feta (Greek cheese)

Table 3 - foods with high concentrations of folic acid

**VITAMIN B6 (pyridoxine):** it can be found both in animal and vegetable products. This vitamin can be deteriorated during cooking processes, packing and refrigeration.

A **1,5mg per day** intake is recommended.

Concentrations	Vegetables and legumes	Fruit	Cereals	Meat and Fish
High concentration of B6 (3-1 mg/100g)			Wheat, cornflakes	
Medium concentration of B6 (0.9-0.2 mg/100g)	broad beans, dried beans, potatoes	Bananas, apples, kiwi, dried prunes, pears	Whole cereals (pasta and rice)	Fish (canned tuna, trout, squid), turkey, lean meats (beef, rabbit), ham, seasoned ham

Table 4 - foods with high concentrations of vitamin B6

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**VITAMIN B12 (cyanocobalamin):** it can only be found in animal products, therefore it is highly recommended to include at least one portion of meat, fish or milk in our daily diet.

A **2µg per day** intake is recommended.

Concentrations	Fish and Meat	Dairy Products	Cereals
High concentration of B12 (20-9 µg/100kg)	Liver, poultry, squid, cod fish		
Medium-high concentration of B12 (9-1 µg/100kg)	Rabbit, horse meat, beef, tuna fish, sardines, mackerel, trout, turbot	Parmesan, feta, mozzarella cheese	Muesli, breakfast cereals
Medium concentration of B12 (1-0.3 µg/100kg)		Milk, ricotta cheese, skim yoghurt	Breakfast crackers

Table 5 - Foods with high concentrations of vitamin B12

### Differences between natural and synthetic vitamins

There is no structural difference between natural vitamins and synthetic vitamins. The only difference is in their bio-availability, thus meaning that there is a difference in the quantity of nutriment that reaches the systemic circulation and

this depends on a number of issues, among which the interaction with other nutriments and with the substances which are normally contained in foods.

Based on the above, we can state that synthetic vitamins are only useful if they are used as an integration and not as a substitute to the dietary intake because they do not have positive synergies with the other substances we can find in food.



### Definition and quantification of portions

A “portion” is a standard quantity of a certain food expressed in grams. This is the measure unit to be used for a healthy diet.

In order to establish how many grams of a certain food or beverage should qualify as a “portion”, the average



consumption of these foods and beverages has been considered for the entire population of Italy in studies

conducted by the National Nutrition Institute (1980-1984) and by ISTAT in 1992 (see Saba et al., 1990; ISTAT, 1992).

The substance of certain packaged products and of single portions on the market have also been considered (LARN, 1996). Along with the above, even the typical products of the Italian diet have been taken into consideration. The weight in grams of the various portions indicated in tables 7-14 has been partially revisited based on the recommended daily assumption of B group vitamins.

### Calculation of quantities based on household measure units: spoons and cups



In our country, the dimensions of many household utensils have changed over the years. The range of traditional spoons (tea spoon, table spoon, dessert spoon, etc.) has been reduced to two elements: a small spoon (for tea and coffee) and a bigger spoon (for broth and soup).

The size of these two spoons is respectively of 5 and 10 cc.

It is therefore possible to measure the portions of foods in terms of table spoons without using a scale, just by knowing the corresponding weight of a full spoon (completely or partially full) for different types of products (see table 6).

Regarding cups, the dimensions of the ones available in Italy are numerous. Since their use is pretty common, a standard cup size has been chosen (generally we use a wine cup, corresponding to 125ml). This measuring unit is very useful for recommendations on liquids.

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Product	Measure unit	Weight in grams
Small pasta	1 full spoon	15
Raw rice	1 full spoon	8
Reggiano Parmesan cheese	1 full spoon	10
Parmesan cheese	1 full spoon	7
Jam	1 partially full spoon	14
Honey	1 partially full spoon	9
Oil	1 partially full spoon	9
Sugar	1 partially full spoon	13
Sugar	1 full spoon	129
Milk	1 full cup	

Table 6 - corresponding weight in grams of certain products measured with 2 household measuring units

### Distribution of food intake during the day

It is important to distribute the assumption of these vitamins during the entire day, starting in the morning:

#### Breakfast

Group of products	Foods	Preferences <sup>4</sup>	Portions <sup>5</sup>	Nr. of daily portions
Milk and Dairy Products	Milk	Cow milk, skim vitamin milk, skim milk	ml 150-200 (1 cup)	1
	Yoghurt	Yoghurt with skim milk, Yoghurt with non fat milk, Yoghurt with whole milk, Fruit flavored yoghurt with skim milk	g 125 (1 jar)	1
Cereals	Breakfast cereals	Cornflakes, oatmeal, muesli, bran flakes	g 30 (3 spoons)	1
		Breakfast crackers, whole wheat cookies	g 30 (nr. 3-5)	1

Table 7 - foods with high presence of B group vitamins

<sup>4</sup> The amount of vitamins is in decreasing order. The products which are not indicated in the graph may be regularly consumed but they will not help in reaching the required daily intake of vitamins.

<sup>5</sup> The concept of portion is the one used in LARN, reviewed and corrected for the aim of these guidelines

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### Lunch/Dinner

Groups of Products	Foods	Preferences <sup>4</sup>	Portions <sup>6</sup>	Nr. of daily portions
Cereals and connected foods	Bread and similar products	Soy bread, brown bread, breadsticks, salted crackers	g 50 (1 sandwich)	2
			g 30 (1 packet)	
	Pasta	Brown rice, bran pasta, white rice	g 80 (1 medium size plate)	1-2

Table 8 - foods with high presence of B group vitamins

Groups of Products	Foods	Preferences <sup>4</sup>	Portions <sup>7</sup>	Nr. of daily portions
Meat	Fresh meat	Rabbit, lean meat, lamb, horse meat, beef, pork, lean steak, chicken	g 130-150 (1 medium size slice)	1
	Preserved meat	Seasoned ham, lean ham	g 70 (7-8 thin slices)	1-2/week

Table 9 - foods with high presence of B group vitamins

Groups of Products	Foods	Preferences <sup>4</sup>	Portions	Nr. of daily portions
Fish	Fresh fish	Squid, trout, mackerel, dogfish, tuna, salmon, shrimps, cuttlefish, sole fish, cod, giltbream	g 150-200 (1 medium size slice)	1
			g 30 (1 packet)	
	Preserved fished	Canned tuna fish in olive oil or in brine	g 80 (1 can)	1-2/week

Table 10 - foods with high presence of B group vitamins

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<sup>6</sup> The quantity is to be halved if it is in soup

<sup>7</sup> The quantity is to be halved if it is in soup

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Groups of Products	Foods	Preferences <sup>4</sup>	Portions	Nr. of daily portions
Eggs	Egg	Chicken egg	g 70 (1 medium size egg)	1-2
Legumes	Fresh	Broad beans, peas, beans	g 100 (5-6 spoons)	
	Dried	Chickpeas, lentils	g 30 (2 spoons)	

Table 11 - foods with high presence of B group vitamins

Groups of Products	Foods	Preferences <sup>4</sup>	Portions	Nr. of daily portions
Milk and dairy products	Fresh cheeses	Spreadable cheese, mozzarella cheese, cottage cheese, sheep milk ricotta cheese	g 100	1-2
	Seasoned	Parmesan, provolone, swiss cheese, blue cheese, Sardinian pecorino cheese, "taleggio" cheese, "fontina" cheese	g 50	

Table 12 - foods with high presence of B group vitamins

Groups of Products	Foods	Preferences <sup>4</sup>	Portions	Nr. of daily portions
Vegetables	Vegetables	Beets, spinach, asparagus, Brussels sprouts, broccoli	g 300	3-5
		String beans, artichokes, courgettes, fennel, sweet peppers, eggplant, tomatoes	g 300	
		Indivia, lettuce heads	g 70	

Table 13 - foods with high presence of B group vitamins

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Groups of Products	Foods	Preferences <sup>4</sup>	Portions	Nr. of daily portions
Fruit	Fruit or juice	Mandarins, kiwi, clementines, oranges, grapefruit, orange juice (packaged, with no sugar), strawberries, bananas, kakis, figs, apricots, cherries, cantalope, grapes, dried prunes, pears, peaches, apples	g 150	2

Table 14 - foods with high presence of B group vitamins

### Consumption frequency

- Consume **3-5 daily portions of vegetables**, including one portion of vegetable soup, and one or more portions to be used as a dressing for pasta and rice (courgettes, eggplants, mushrooms, fresh tomatoes, artichokes, asparagus, etc.)
- The **2-3 portions of fruit** or of fresh juice may be consumed aside from regular meals
- **Cereals and similar products** (bread, pasta, rice, etc.) must be consumed every day in the indicated portions. Oven cooked products may be consumed for breakfast and aside from regular meals
- Regarding weekly **main courses**, we suggest the following consumption frequencies: 3-4 portions of fish, 2-3 portions of meat, 2 portions of cheese, 1-2 portions of eggs, 1-2 portions of cold cuts. At least 1-2 times per week, the main course must be substituted with a single dish based on cereal products (pasta, rice, spelt, barley, etc.) with legumes (beans, peas, chickpeas, lentils, etc.) in the indicated portions for each product
- **Milk and/or yoghurt** must be consumed every day (2 portions per day). One cup of milk is equal to 150/200ml
- As a dressing, olive oil is highly recommended (better if it's extra-virgin oil)



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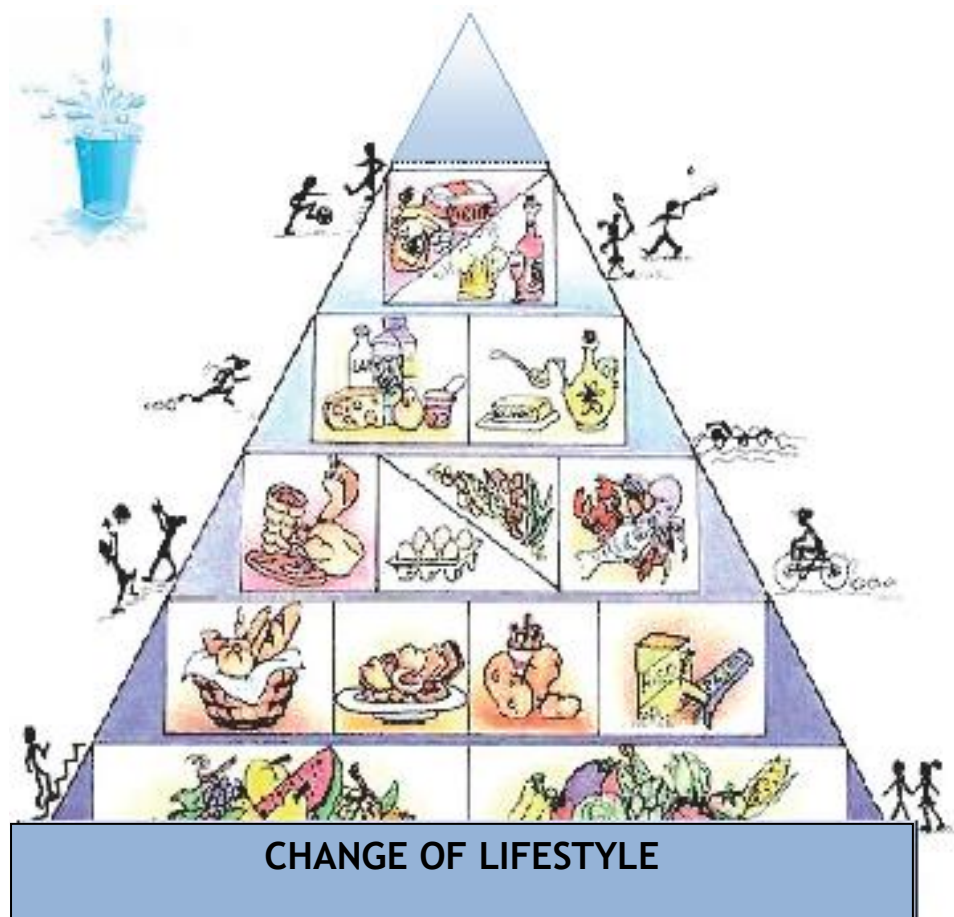
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### The food pyramid

Based on what we have stated here above, we hereby propose a food pyramid that is based not on cereals, but on fruits and vegetables.

As you can see water has been inserted on the side: it must never go missing in our daily diet.

It is important to drink based on our thirst and always remembering to drink at least 1.5/2 liters per day.



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### Varying our diet

Here following is an example of a balanced dietary scheme with Vitamins B and folic acid:

1600 Kcal scheme		2100 Kcal scheme	
Product	Portion (g)	Product	Portion (g)
<b>Breakfast</b>		<b>Breakfast</b>	
Skim milk	200	Skim milk	200
Vitamin biscuits	30	Vitamin biscuits	30
<b>Snack</b>		<b>Snack</b>	
crackers	30	crackers	30
<b>Lunch</b>		<b>Lunch</b>	
Whole wheat bread	50	Whole wheat bread	50
Fish/meat	150/130	Pasta with	80
Cooked vegetables	300	vegetables	200/150
Fruit	150	Fish/meat	300
<b>Snack</b>		<b>Snack</b>	
Yoghurt	125	Yoghurt	125
<b>Dinner</b>		<b>Dinner</b>	
Whole wheat bread	50	Whole wheat bread	50
Pasta	80	Pasta with	80
with fresh legumes	100	vegetables	100
Raw vegetables (e.g. tomatoes)	250	Fresh cheese	80
Fruit	150	Raw vegetables	150
		Fruit	

Table 15 - dietary scheme with vitamins B6 (equal to 2.5mg), B12 (equal to 2 µg), folic acid (equal to 685 µg)

Product	1600 KCAL	2100 KCAL
	Portions	Portions
Milk and dairy products	2/day	2/day
Bread and cereals	4/day	5/day
Legumes	1-2/week	1-2/week
Fish/meat	1/day	1/day
Vegetables	3/day	4/day
Fruit	2/day	2/day

Table 16 - consumption frequencies for certain food products

The two explanatory dietary schemes shown in table 15 are based on the number of portions of food that must be consumed for each food category in one day.

### When is an integration necessary?

There are particular situations in which our need for vitamins is not satisfied by our diet. In these cases, we must provide our body with a supplementation. The above may happen when particular physio-

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pathological conditions are present, for example during pregnancies, during menopause, during periods of elevated stress both physical and mental, in presence of hyperhomocysteinemia. We can use generic multi-vitamin integrators (these usually contain other important vitamins such as vitamins A, C, D and minerals such as Zn and Fe), or we can use aimed integrations.

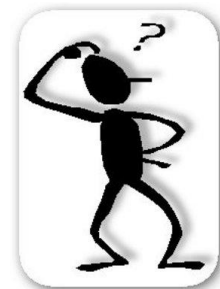
In case of **hyperhomocysteinemia**, it is **highly recommended** the patient follows a balanced diet, enriched with vitamins B6, B12 and folic acid and, if this were not sufficient, an **aimed vitamin integration with vitamins B6 (2mg), B12 (1µg), folic acid (300µg)** could also be helpful.

### Fortified foods

Foods in which folic acid and vitamins B6 and B12 have been added are available on the market. These can increase the daily intake of these micro-nutriments. It is important to keep in mind that this enrichment must be indicated in the nutritional info on the package by law (Reg. CE 1925/2006). In Italy, only certain fortified foods are available. For example, we can find fortified breakfast cereals (cereal bars and cornflakes), fortified juices, a special UHT milk and certain types of yoghurt.

### How to read nutritional info

It is important to check the list of **folic acid** or folacin or **vitamin B9**, **vitamin B6** or pyridoxine and **B12** or cyanocobalamin contents on the food package. If this information is not indicated on the package, the product does not contain these micro-nutriments or that it has not been fortified.



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