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SELECTIVE ADMINISTRATION OF POLYAMINE-DEFICIENT AND POLYAMINE-FREE DIETS TO CANCER PATIENTS

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Abstract

Aliphatic polyamines (putrescin, spermidine, spermine and cadaverine) play an important role in the induction of neoplastic processes leading to cell malignancy. In malignantly transformed cells, a high level of aliphatic polyamines has been observed, which ensures their steady anaplastic growth. This is precisely why elevated levels of the aforementioned polyamines are considered as diagnostic and prognostic criteria for a wide range of oncological diseases.

In several developed countries, cancer patients are advised to follow a low-polyamine diet, including specifically those food products that are identified in the general nutrient registry as having low levels of aliphatic polyamines.

However, when recommending such a diet, many researchers did not pay attention to the fact that in different food products, the ratio of polyamine levels often varies within very wide limits. Therefore, as some researchers report a polyamine-deficient diet prescribed to cancer patients is not always effective.

We analyzed various literary sources and identified products that do not contain polyamines or contain them in very low quantities.

Based on the analysis of available literary data, when patients are admitted to oncology clinics, along with generally accepted laboratory diagnostic criteria, it is necessary to include diagnostic indicators for determining the levels of aliphatic polyamines in erythrocytes and blood plasma, including putrescine, spermidine, spermine, and cadaverine.

Due to this approach, oncologists and nutritionists may have a real opportunity to prescribe a selective polyamine-deficient diet. For patients with advanced cancer, we recommend the use of a polyamine-free diet instead of a polyamine-deficient one.

Keywords: *oncological diseases, malignant tumors, aliphatic polyamines, polyamine-deficient diet, polyamine-free diet.*

Introduction

Studies of the last forty-five years have revealed that polyamines have a modulating effect on reparative-proliferative processes in tissues of various origins in mammals.

The impaired metabolism of polyamines (putrescin, spermidine, spermine and cadaverine) in epithelial and mesenchymal tissues is frequently observed as a provoking factor causing hyperplastic processes in parenchymal organs as well as in organs of immunogenesis. Nevertheless, it is a well-known fact, that hyperplastic processes are considered to be the risk factors for both the occurrence of malignant tumors and/or the transformation of benign tumors into malignant ones.

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1. Role of aliphatic polyamines in certain malignant neoplasms

Polyamines (putrescin, spermidine, spermine, cadaverine and agmatin), γ- and α-synucleins are currently the subject of a special comprehensive study due to their direct influence on the formation of neoplastic processes. Many advanced scientists began their fundamental research at the end of the last century contributing considerable input in studying the role of polyamines in the pathogenesis of malignant neoplasms [*Volkov N et al., 1983; Moulinoux J et al., 1984a; Jensen J et al., 1987; Moulinoux J et al., 1989a; Moulinoux J et al., 1989b; Avagyan S et al., 2022b*]. Thus, it was found out that in increased cell proliferation under normal conditions, and especially in malignantly regenerated cells, rather high concentrations of polyamines are determined in their cytoplasm [*Jänne J et al., 1978; Volkov N et al., 1983; Moulinoux J et al., 1989a; Sarhan S et al., 1989*]. Addition of polyamines to cell culture medium, where proliferation processes were previously inhibited, markedly restored their mitotic activity. In this regard, the studies of Sarhan 1989, in which polyamines from "exogenous" medium are shown to accumulate exclusively in tumor cells, deserve special attention, in our opinion. Equally informative research revealed that while feeding laboratory animals with food deprived of polyamines, as well as introducing inhibitors of polyamine biosynthesis into food, significantly inhibits proliferative processes in malignant neoplasms induced in rats [*Sarhan S et al., 1989; Seiler N et al., 1990*].

Particular attention should be paid to the fact that both red blood cells in patients suffering from various malignant diseases and red blood cells of laboratory animals with induced neoplastic process are characterized by significantly elevated polyamine levels [*Moulinoux J et al., 1989a; 1989b 1987*]. The presence of noticeably significant high concentrations of polyamines in the cytoplasm of erythrocytes has currently no distinct explanation, especially since mammalian erythrocytes lack ultrastructure responsible for synthetic processes. In our opinion, the assumption of Moulinoux I. (1984 a, b), that red blood cells characterize the levels of polyamines which are released by cancer cells is of particular interest. However, Quemener V. (1990) put forward another hypothesis, according to which erythrocytes can act as a "polyamine reserve" for cancer cells in mammals [*Moulinoux J et al., 1984a; 1984b; Sarhan S et al., 1989; Avagyan S et al., 2022b*].

The fact that high polyamine content is found not only in cancer cells, but also in erythrocytes suggests broad prospects for both the early diagnosis and prognosis of malignant diseases by studying polyamines in the erythrocytes of patients' blood, since there is a direct correlation between high concentrations of polyamines in cancer cells and red blood cells.

Malignant neoplasms still remain the second most common cause of morbidity and mortality in the world. Every year, millions of new cancer cases are recorded all over the world, with the most common being breast cancer, prostate cancer, colorectal cancer, lung cancer, malignant neoplasms of the reproductive organs, etc. According to the data summary, the treatment effectiveness of malignant diseases varies significantly, depending on the tumor type [*Wallace HM et al., 2003*]. Thus, with a five-year survival rate for breast cancer, the rate of successful therapy is 80-90% and 45-55% for colorectal cancer, but is much lower for lung cancer, constituting 5-15%.

As we have indicated above, the new highly informative data appear periodically, indicating the important role of polyamines in pathogenesis of many malignant diseases. In this regard, certain amendments, concerning the peculiarities of polyamine metabolism and their accumulation in malignantly reborn cells, continue to be included in the general treatment scheme of oncological diseases (often in the form of "protocols"). Wallace H.M. (2009), one of the founders of the polyamine theory, therein considers four fundamental criteria that should be taken into account when studying various aspects related to the role of polyamines in the induction of oncological diseases:

- Polyamines are essential for cell growth;
- The concentration of polyamines increases significantly in malignantly reborn cells;
- Ornithine decarboxylase should be considered as an oncogene (co-oncogene);
- Interventions, associated with the inhibition of polyamine synthesis prevent cancer cell growth.

It would hardly be an exaggeration to say that all the attempts to find new means of symptomatic

and pathogenetic therapy of malignant neoplasms, related to the polyamine metabolism disruption, are based on the tenets mentioned in the paragraphs above [*Wallace H, 2009*].

Polyamine content in malignant human cells is several times higher than in the parent normal cells. In this respect, indicators that are presented in the early studies appear to be very demonstrative [*Kingsnorth A et al., 1994a; 1994b*]. Breast cancer cells thus contain 6 times more polyamines than is found in normal breast cells. A similar pattern is also observed in colon cancer, in which the content of polyamines in malignantly regenerated cells is 3-4 times higher than in normal colon cells. Along with the high level of polyamines in cancer cells, the activity of ornithine decarboxylase, the fundamental enzyme that converts ornithine to putrescine, also increases. High levels of polyamines (putrescine, spermidine and spermine) and high ornithine decarboxylase activity are observed in certain hyperplastic processes, benign and malignant tumors localized in the organs of the gastrointestinal tract and reproductive system [*Luk G, Baylin S, 1983; Garewal H et al., 1988; Verma A,1990; Fernández C et al., 1995; Jeon J et al., 2003; Bassiri H et al., 2015*].

There is also research of considerable interest, focused on aliphatic polyamines as risk factors in inducing cervical cancer associated with sexual behavior. Thus, Fletcher S. (1991) studied the effect of aliphatic polyamines, identified in seminal fluid, upon the cell cycle as well as ploidy of cervical cells and "primary" epithelial cells, cultured from cervical biopsy samples. The cell growth processes were not impaired, however, in a number of samples, signs of hypodiploidy or hyperdiploidy were observed, depending on the concentration of spermine and spermidine in the seminal fluid [*Fletcher S et al., 1991*]. The authors believe that there is an interaction between polyamines of seminal fluid and the DNA of uterine mucous cells, which leads to the ploidy changes, which is often fraught with the development of dysplasia. Clinicians and primarily oncologists and sexopathologists should pay special attention to the fact that the pathogenesis of cervical cancer is conditioned not only by the persistence of the human papilloma virus in situ. It is a known fact that seminal fluid is relatively rich in putrescine, spermidine and spermine. A number of authors attempted to identify the role of seminal fluid polyamines as cofactors in the development of cervical cancer [*Saydjari R et al., 1989; Dunzendorfer U, Russel D, 1978; Fernández C et al., 1995*]. The research of many authors are based on the well-known fact, that aliphatic polyamines (putrescine, spermidine and spermine) undergo oxidation by polyamine oxidase and diamine oxidase, with the formation of oxygen radicals, hydrogen peroxide and reactive aldehydes, which apparently can cause cytotoxic, mutagenic and immunosuppressive in situ effects on the cervical mucosa. According to these results, the authors came to a quite reasonable conclusion that high levels of polyamine oxidase and diamine oxidase in the cervical mucosa should be considered an increased risk factor for cervical cancer, especially in cases with high concentrations of putrescine spermidine and spermine detected in the seminal fluid. However, some authors are quite right to assume that "papilloma-virus infection might synergize the effects of polyamine oxidation, suppressing apoptosis in uterine mucosa cells, carrying potentially oncogenic mutations, which leads to the survival and proliferation of transformed cervical cells," in other words, resulting in their malignancy.

Kim et al. (2005) presented some data on the diagnostic significance of polyamines, particularly in predicting the risk of metastases to the lymph nodes in squamous cell carcinoma of the cervix. There are informative data on the role of aliphatic polyamines and ornithine decarboxylase in the induction of benign and malignant tumors of the pancreas [*Dunzendorfer U, Russel D, 1978; Feuer E et al., 1995; Simoneau A et al., 2003, Kim Y et al., 2005*]. Moreover, it is known that in pancreatic cancer the level of aliphatic polyamines – putrescine, spermidine and spermine in the pancreas is undoubtedly very high, the activity of ornithine decarboxylase is much higher than in benign tumors localized in other organs [*Dunzendorfer U, Russel D, 1978; Devens B et al., 2000*].

There are highly informative data on the shifts in the polyamine system, which are considered objective criteria for the diagnosis and prognosis of a number of malignant tumors [*Lipton A et al., 1975; Rudman D et al., 1979; Garnica A et al., 1982; Saydjari R et al., 1989; Lawton F et al., 1990; Os-*

swald H et al., 1998; Liu R et al., 2012]. A number of authors examined 39 patients with ovarian cancer to determine polyamine levels in the urine [*Lawton F et al., 1990; Liu R et al., 2012*]. From the total number of patients, 20 were resistant to chemotherapy. In resistant patients, high rates of putrescine and spermine fractions were revealed in the urine. In other cases, when the therapy was effective, high spermidine levels were found in urine in addition to high levels of putrescine and spermine. Conducted researches highlight the important role putrescine might play in paraclinical diagnostics of malignant neoplasms. In the plasma of healthy volunteers and patients with a number of malignant tumors, the content of diaminopropane, putrescine, spermidine and spermine was determined by high-performance column chromatography. As the study results showed, rather high indices of the above-named polyamines were determined in the plasma of patients with malignant neoplasms as compared to the values recorded in the plasma of healthy volunteers. The authors concluded that the observed spectrum of polyamines should be considered as diagnostic criteria in the clinical trials for malignant tumors. Uehara N. (1990a) came to a similar outcome in determining erythrocyte levels of spermidine and spermine in patients with malignant tumors, considering the levels of these polyamines as markers of the activity of the pathological process. Horn et al. (1982) investigated 190 patients with various malignant tumors over a relatively long time, with strict adherence to the conditions of relevant protocols [*Horn Y et al., 1982; Uehara N et al., 1990a*]. Taking into account the active and inactive phase of the cancer course, the levels of putrescine, spermidine and spermine in the urine of patients were determined. The authors concluded that the serial determination of polyamine levels in the urine might have clinical application for monitoring a number of oncological diseases.

While studying metastatic tumors of the gastrointestinal tract, different levels of specific polyamines (putrescine, spermidine and spermine) were found in the urine of patients, depending on the nature and location of tumors in the abdominal cavity and pelvic area [*Lipton A et al., 1975; Russel D et al., 1978*]. As noted by the authors, spermidine and spermine indices determined in rather high concentrations among the patients observed, turned out to be more informative. A noteworthy fact is that shifts in the polyamine content in the urine of patients suffering from various forms of lymphomas can serve as additional diagnostic criteria in "Hodgkin's" vs. "non-Hodgkin's" lymphomas [*Thyss A et al., 1982*]. Thus, in Hodgkin's disease, certain patterns of specific polyamine shift in urine were not detected. Meanwhile, these consistent patterns were revealed in other forms of lymphomas, which made it possible to assess the significance of the polyamine shifts as the chemotherapy positive effect estimate. Research carried out by Uehara (1990b) also deserves some attention. In various oncological diseases, Uehara N. and co-authors determined the polyamine levels not in urine and plasma, but in erythrocytes. The authors assume that relatively high levels of spermidine and spermine in erythrocytes in patients with malignant tumors (as compared with erythrocytes in the blood of healthy volunteers) might be clinical markers of the pathological process severity. The important role of specific representatives of the polyamine system in the induction of the tumor process was pointed out in the experimental studies, carried out by a group of authors [*Russel D et al., 1974; Uehara N et al., 1990b*].

The most informative and fundamental research in terms of studying the role of polyamines in a wide range of oncological diseases was the one carried out by a group of authors [*Russel D et al., 1974; 1975; 1977*]. In all the above studies, the key point that stands out is that levels of polyamine excretion in urine are considered to be cancer monitoring criterion on the one hand, and an early cancer detection test on the other hand. Based on the fundamental research in this field, the authors propose a hypothesis that polyamines should be observed as clinical indicators to monitor the treatment of malignant tumors; herewith, spermidine only can be considered a "marker of tumor cell death" while putrescine appears to reflect the "proliferative behavior" or "growth fraction" of a tumor [*Russel D et al., 1975*].

Conversely, an opposing view exists regarding the changes in the content of polyamines in the cerebrospinal fluid and serum, observed as diagnostic criteria for neoplastic growth in brain

structures. Fulton et al. (1982) studied the polyamine content shifts in the cerebrospinal fluid of patients with malignant tumors and in a number of neurological diseases, in which there were no signs of neoplastic growth in the hypophysis. In a comparative analysis of cerebrospinal fluid samples, significant changes in the content of putrescine and spermidine were not found. Approximately the same indicators of polyamines under study were determined in all of the groups observed. The authors conclude that shifts in the content of the studied polyamines cannot be considered as diagnostic criteria for the development and course of neoplastic processes in the hypothesis [*Fulton D et al., 1982*].

2. Some new approaches of symptomatic therapy and prophylaxis of oncological diseases

The search for effective agents that suppress polyamine synthesis in a number of oncological diseases was aimed at inhibiting specific enzymes, directly involved in the general cascade of reactions in charge of the step-wise synthesis of specific polyamines – ornithine decarboxylase, adenosylmethionine decarboxylase [*Stanek J et al., 1992; Seiler N, 2003*].

Ornithine decarboxylase in mammals acts as the only "launcher" enzyme for the formation of putrescine from ornithine, as indicated previously. That is why the research in practical oncology, aimed at finding new effective means of inhibiting the activity of ornithine decarboxylase appeared to be the most productive [*Metcalf B et al., 1978*]. The most effective blocker of this class of drugs is the "irreversible" ornithine decarboxylase inhibitor i.e. α-difluoro-methyl-ornithine (DFMO) [*Meyskens F, Gerner E, 1999*].

The twenty-year experience in DFMO testing was a precondition for searching and developing polyamine analogues in oncology that should compete with endogenous polyamines (putrescine, spermidine and spermine) by inhibiting the activity and biosynthesis of ornithine decarboxylase.[15] In our opinion, the studies on the therapeutic efficacy of DFMO in the "treatment" of cervical intraepithelial neoplasia are of considerable interest. Boiko G.V. (1998) studied the effect of DFMO on the expression of epidermal growth factor, which is known to be a marker of cervical intraepithelial neoplasia progression. As the research results showed, the localization of the epidermal growth factor is limited to the basal layer of the epidermis in the normal (control) epithelium, whereas in case of cervical intraepithelial neoplasia, the expression of the epidermal growth factor was more common and spread to other, more superficial layers of the epidermis. The DFMO application for therapeutic purposes in cervical intraepithelial neoplasia limited the distribution of epithelial receptors to the epidermal growth factor significantly. This allowed the authors to conclude that the progression of cervical neoplasia is associated with spatial dysregulation of the epidermal growth factor, which can be reversed by using DFMO. The considerable therapeutic efficacy of DFMO was revealed in the research of a number of authors in complex therapy of patients with grade III cervical intraepithelial neoplasia [*Boiko G et al., 1998; Mitchell M et al., 1998*]. The use of DFMO was accompanied by a decrease in the spermidine/spermine tissue index and an increase in the level of ornithine in the plasma of the patients with cervical neoplasia. According to the authors, the use of DFMO for therapeutic purposes in various increasing doses did not cause toxic disorders in patients with III severity degree of cervical neoplasia. The efficacy of DFMO application was also revealed in the complex treatment of multiple adenomas, which prevented significantly the risk of colorectal neoplasia [*Laukaitis C, Gerner E, 2011*]. Based on previously conducted experimental and clinical studies (including their own research), the scientific elaboration of Bassiri et al. (2015) on the use of specific doses of DFMO in the neuroblastoma complex therapy in children deserves special attention [*Bassiri H et al., 2015*]. The noteworthy fact is that the symptomatic and pathogenetic therapies of a number of oncological diseases are carried out due to the increasing use of endogenously active substances or their synthetic analogues, since it is the endogenous biological factors that, under the conditions of impaired in situ metabolism, largely determine the nature and features of many oncological diseases.

There is also another approach in which a "low polyamine diet" is recommended for cancer patients. Some positive results achieved by using a

similar diet in hormone resistant prostate cancer.[15, 53,54] This approach is believed to be highly promising in oncology. The assumption we have put forward is highly valid, since the levels of polyamines in numerous food and alcohol products vary within rather wide limits.

Along with numerous social factors, adherence to the correct diet, balanced nutrients containing proteins, fats and carbohydrates is one the factors that contribute to the high quality of life. The combination of natural food products with various preservatives, flavor compounds, natural ingredients being artificially replaced, as well as the introduction of food additives have an unfavorable effect on human health.

In the development of several pathological conditions, including neurological diseases and disorders (Parkinson's disease, epilepsy, dementia, and autism), cardiovascular diseases (including acute and chronic ischemic heart disease, dilated cardiomyopathy, and ischemic cardiomyopathy), and certain viral infections (HIV infection, COVID-19, papillomas), polyamine metabolism, particularly involving aliphatic polyamines like putrescine, spermidine, spermine, and cadaverine, may play a significant role.

3. The role of polyamines entering the body through food intake

The polyamines (putrescine, spermidine, spermine and cadaverin) are present in variable amounts in almost all kinds of food [*Bardócz S et al., 1993; Okamoto A et al., 1997; Bardócz S, White A, 1999; Deloyer P et al., 2001*]. The daily polyamine intake for adults is estimated to vary between 350 and 550 μmol [*Bardócz S et al., 1993; Okamoto A et al., 1997; Deloyer P et al., 2001*]. The effects of these dietary polyamines on the growth and disease in animals and humans, either at postnatal or adult stages was thoroughly analyzed in the study of Deloyer P. (2001) and Avagyan S et al., (2022a).

In addition to medication-assisted treatments for individuals diagnosed with the aforementioned diseases, significant emphasis is placed on their dietary management. Various dietary strategies are employed to create personalized food plans. In recent years, particular focus has been directed towards the polyamine diet, which involves daily consumption of food products rich in polyamines. The polyamine diet is recommended for preventive measures, both to maintain a healthy lifestyle and during the treatment of a number of diseases [*Zoumas-Morse C et al., 2007; Avagyan S et al., 2022a*].

It is important to note that among the diseases in which impaired metabolism of aliphatic polyamines plays a significant role (as we mentioned above), oncological diseases are also included. In several oncology clinics, as part of medication-assisted treatment, patients are advised to strictly adhere to a polyamine-deficient diet.

In many countries, a registry of food products has been established based on their aliphatic polyamine content, as summarized in the publication (Table 1).

In several European and Asian countries, cancer

Table 1

Estimated average intake of polyamines (μM*/day*) in different studies [Muñoz-Esparza N et al., 2019]

Country	Polyamines				References
	Total (*g/day*)	Put (*μM/day*)	Spd (*μM/day*)	Spm (*μM/day*)	
European Union	353.6	211.9	87	54.7	Ralph A et al., 1999
United Kingdom	315.1	160.3	96.7	58.1	
Finland	343.6	222.6	71.9	49.1	
Sweden	362.9	250.5	70.0	42.3	
Spain	384.3	211.7	103.1	69.5	
Italy	387.7	247.4	83.6	56.7	
Japan	200	90	74	36	Nishibori N et al.2007
USA	249.5	159.1	54.7	35.7	Zoumas-Morse C et al., 2007
Sweden	316	215.5	66	34.5	Ali AM et al., 2011
Turkey	139.9	93.1	33.1	13.7	Buyukuslu N et al., 2014

TABLE 2

Polyamine concentrations (*nmol/g*) in food products for diet groups [*Soda K et al., 2009*]

	Put	Spd	Spm	Total
Low polyamine diet	496	224	143	863
Normal polyamine diet	625	434	160	1219
High polyamine diet	1075	1540	374	2989

Notes: *Put – putrescine, Spd – spermidine, Spm – Spermine*

patients are advised to follow a polyamine-deficient diet. The preparation of a polyamine-deficient diet is guided by grading food products according to their aliphatic polyamine levels (Table 2).

Based on data provided by Phan N. (2011), Kuniyasu S. (2012), and Cipolla B. (2010) and their co-authors, a list of food products for cancer patients was categorized according to their varying aliphatic polyamine content. The first group comprised products with very low polyamine content (less than 100 *nmol/g*), the second group included products with polyamine levels ranging from 101 to 200 *nmol/g*, and the third group – products with a relatively high polyamine content, exceeding 201 *mmol/g* (Table 3) [*Kuniyasu S et al., 2009; Phan N et al., 2011; Cipolla B et al., 2010; Avagyan S et al., 2022a*].

In several studies on the treatment of malignant neoplasms, it has been recommended to use an enzyme ornithine decarboxylase inhibitor, which is a key enzyme in the synthesis of putrescine from ornithine, alpha-difluoromethylornithine (DFMO). However, it's important to note that drugs developed based on DFMO are not always effective.

According to our proposal, when prescribing DFMO, the levels of specific aliphatic polyamines in the patients are not always taken into account. For instance, if a cancer patient has an elevated level of putrescine while simultaneously having a reduced level of cadaverine in their blood, the use of DFMO or its medicinal analogs may be effective. Conversely, when high levels of cadaverine and low levels of putrescine are detected, the use of DFMO is ineffective.

In the case of using various polyamine-deficient diets, we have analyzed the levels of individual polyamines in different food products that, in our opinion, deserve special attention (Table 4) [*Shrestha R et al., 1992Cipolla B et al., 2010 Büyükuslu N, 2015*].

For example, in apricots and dried milk, the total amount of polyamines is approximately the same, around 15.0 and 16.0 *mmol/g*, respectively. However, in the first product, the level of putrescine is 8.0 *mmol/g*, while in the second product, it is 2.0 *mmol/g*. Spermine is not detectable in apricots, but in dried milk, it is 7.0 *mmol/g* [*Bardócz S et al., 1993; Okamoto A et al., 1997; Bardócz S, White A, 1999; Ralph A et al., 1999; Cipolla B et al., 2003; Cipolla B et al., 2007; Avagyan S et al., 2021; Avagyan S et al., 2022a*].

In our opinion, based on these indicators it becomes evident that the use of apricots cannot be recommended for cancer patients who already have elevated putrescine levels, despite it being considered a polyamine-deficient product.

TABLE 3

Polyamine contents in regular food [*Cipolla B et al., 2003*]

Permitted every day (<100 *nmol/g*)	Permitted once in a while (101-200 *nmol/g*)	Forbidden (>201 *nmol/g*)
Bread	Yoghurt	Carrots
Meats, beef, veal, pork, poultry	Pasteurized cheese	Radishes
Eggs	Jams	Celery
Fish (fresh)	Wine	Green beans
Milk and white cheese		Oranges and juice
Pasta and rice		Bananas
Tomatoes, onions, mushrooms, lettuce, spinach, potatoes, beetroot		Prunes
		Grapefruit
Apples, pears, peaches, strawberries, grapes		Melon
		Liver
Flour, margarine, butter, oil		Fermented cheese: stilton, Roquefort, gorgonzola, camembert
Salt and pepper		
Biscuits		
Water, coffee, tea		

Table 4

Products (a partial list) that can be consumed in a polyamine-deficient diet [*Cipolla B et al., 2003*]

Food products	Put	Cad	Spd	Spm	Total
White wine (Burgundy)	9.0	bdl	1.0	bdl	10.1
Apple juice	11.1	bdl	2.0	bdl	13.1
Grape juice	9.0	bdl	5.1	bdl	14.1
Apricot juice	8.0	bdl	7.0	bdl	15.0
Dried milk	2.0	bdl	7.0	7.0	16.0
Prune	6.1	1	10.1	2	19.2
Pear	0.4	0.7	18.4	0.2	19.8
Freshly-laid egg	20.5	bdl	bdl	bdl	20.5
Pear	4.3	0.7	20.3	bdl	25.3
Stout beer	21.2	1.0	bdl	bdl	22.2
Red table wine (Bordeaux)	22.3	bdl	bdl	bdl	22.3
Peach	7.4	1.0	18.4	bdl	26.8
Egg yolk (freshly-laid)	43.7	bdl	bdl	bdl	43.7
Onion	5.7	3.3	35.4	bdl	44.3
Diced bacon	3	12.1	7.0	26.3	48.3
Tomato juice	35.5	1.0	13.2	1.0	50.7
Apple	30.3	0.9	22.1	bdl	53.3
Semolina	25.1	1.0	5.0	23.1	54.2
Red grapes	34.2	6.4	15.2	0.1	55.8
Fresh pasta	13.0	3.0	35.1	6.0	57.1
Green pepper	21.6	5.3	30.4	4.1	61.4
Normal ripe carrot	7.7	0.8	53.6	2.7	64.8
Toulouse sausage	3.0	1.0	16.3	46.2	66.5
Green cabbage	6.0	1.0	55.7	6.4	69.1
Spicy sausage (merguez)	8.1	1.0	12.2	48.3	69.6
Lemon	53.8	0.8	18.4	0.9	73.8
Strawberry	18.5	4.3	40.3	13.7	76.8
Chipolata	3.0	1.0	24.2	50.3	78.5
Beet, beetroot	51.7	0.2	29.1	bdl	81.0
Frankfurter sausage	11.1	14.2	27.0	31.1	83.4
Skinned potato	31.4	5.1	46.1	4.3	86.8
Pork (roast)	4.0	3.0	9.3	72.3	88.6
Turkey (wing)	14.1	2.0	10.1	68.3	94.5
White bread	13.0	15.3	54.2	13.2	95.7
String beans	65.2	bdl	27.2	6.0	98.4

Notes: *Put - putrescine, Spd - spermidine, Spm - Spermine, Cad - cadaverine, bdl- below detection limits*

That's why nutritionists and attending oncologists should have data on the levels of aliphatic polyamines in plasma and red blood cells as a diagnostic marker for each cancer patient in their toolkit. It's also advisable to use charts that display polyamine levels in the diet specific to a particular geographic region.

Unfortunately, there is no standardized diet plan that presents aliphatic polyamine levels based on geographic regions. An exception is the study by Büyükuslu et al. (2014), which introduced a polyamine-containing diet specific to the Middle Asian region [*Büyükuslu N et al., 2014; Büyükuslu N, 2015; Avagyan S et al., 2022a*].

When analyzing the data from many researchers, certain food products are clearly identified in which the presence of aliphatic polyamines has not been detected (Table 5), or their total amount was very low, i.e., less than 10 *nM/g*. Such food products can be considered polyamine-free.

A diet consisting of polyamine-free food products can be recommended as a polyamine-free diet. In our opinion, a polyamine-free diet should be recommended for cancer patients with a severe disease course or for those patients who have not undergone polyamine laboratory diagnostics.

It is also worth noting that a relatively high level of aliphatic polyamines is detected in the soft tissues of skin wounds. According to some authors,

Table 5

Polyamine-free products

Food products	Put	Spd	Spm	Cad	Total
Butter	bdl	bdl	bdl	bdl	bdl
Salt	bdl	bdl	bdl	bdl	bdl
White pepper	bdl	bdl	bdl	bdl	bdl
Black coffee	bdl	bdl	bdl	bdl	bdl
Ceylon tea	bdl	bdl	bdl	bdl	bdl
Champagne cider	bdl	bdl	bdl	bdl	bdl
Cola beverage	bdl	bdl	bdl	bdl	bdl
Curdled milk	bdl	bdl	bdl	bdl	bdl
Skimmed milk	bdl	bdl	bdl	bdl	bdl
Cream	bdl	1	bdl	bdl	1
Milk (semi-skinned, low fat)	1	bdl	bdl	bdl	1
Natural yoghurt	0.3	0.4	0.4	bdl	1.1
Egg white (freshly-laid)	1	bdl	bdl	bdl	1.0
Whisky	bdl	1	bdl	bdl	1
Cognac	bdl	1	bdl	bdl	1
Rice (white)	2.0	bdl	bdl	bdl	2.0
Soft cheese	bdl	1	1	1	3
Caster sugar	3	bdl	bdl	bdl	3.0
Very thin pancake (crepe)	bdl	5	1	1	7.0
Chocolate eclair	2	3	bdl	2	7.0
Wine vinegar	8	bdl	bdl	bdl	8.0
Mayonnaise	1	4	1	3	9.0
Honey	8	1	bdl	1	10.0
Cookie (sweet biscuit)	2	6	1	1	10.0

Notes: *Put - putrescine, Spd - spermidine, Spm Spermine, Cad - cadaverine, bdl- below detection limits.*

in such a situation, as in situ proliferative processes intensify, the risk of developing skin malignant neoplasms increases significantly [*Gilmour SK, 2007; Nowotarski S et al., 2015; Avagyan S et al., 2021; 2022a; 2022b*].

4. Polyamine diet for a number of somatic diseases

It is important to note that, apart from cancer, we also advocate a polyamine-deficient diet for various somatic diseases of both infectious and non-infectious origins. These conditions involve impaired metabolism of aliphatic polyamines – specifically putrescine, spermidine, spermine, and cadaverine in their pathogenesis. This diet is specifically recommended for diseases such as Parkinson's disease, hemorrhagic and ischemic strokes, dilated idiopathic and ischemic cardiomyopathy, Covid-19, and chronic wound infections, where there is a significant elevation in the levels of polyamines in patients.

A polyamine diet can also be used for diseases characterized by a significant increase in aliphatic polyamine levels, also due to metabolic disorders. Unfortunately, information about elevated levels of polyamines in many somatic diseases is lacking. However, we firmly consider it a proven fact that in autistic disorders, the level of polyamines is significantly lower. These indications can also serve as diagnostic criteria for the classification of these disorders.

Conclusion

In conclusion, we recommend the creation of a "diagnostic card" for each cancer patient, which should include measurements of aliphatic polyamines – putrescine, spermidine, spermine, and cadaverine in both plasma and red blood cells.

For this purpose, it is necessary to have specialized biochemical laboratories in oncological institutions to measure the aforementioned aliphatic polyamines.

Based on the laboratory analysis results, nutritionists and oncologists are advised to selectively prescribe a polyamine-deficient diet for cancer patients. In particularly severe cases of the disease, the use of a polyamine-free diet can be recommended. Additionally, it is recommended to consider a polyamine-free diet for cancer patients who did not undergo diagnostic analysis for aliphatic polyamines before treatment.

REFERENCES

1. *Ali A, Poortvliet E, Stromberg R, Yngve A. (2011)*. Polyamines in foods: development of a food database. Food Nutr. Res. 2011; 55: 1-15
2. *Avagyan S.A., Zilfyan A.V., Muradyan A.A., Gazaryan H.V. (2022).* Potential significance of aliphatic polyamines, α-synucleins and Helicobacter Pylori in diagnostics and prognosis of some malignant tumors. The New Armenian Medical Journal, 16(4): 41-53, https://doi.org/10.56936/18290825-2022.16.4-41
3. *Avagyan SA, Zilfyan AV, Muradyan AA (2021)*. The need to add a "polyam ine-deficient" diet in the food registry of COVID-19 pat ients, The New Armenian Medical Journal, Vol.15 (2021), No 2, p. 19-34
4. *Avagyan SA, Zilfyan AV, Muradyan AA (2022)*. New approaches related to the use of polyamine-free and polyamine-deficient diets in the list of nutritional products for COVID-19 patients; NAMJ v.16 (2022) no.6, p. 14-24; DOI: https://doi.org/10.56936/18290825-2022.16.2-14
5. *Bardócz S, Grant G, Brown DS, Ralph A, Pusztai A. (1993).* Polyamines in food – implications for growth and health. J Nutr Biochem. 1993; 4: 66-71
6. *Bardócz S. and White A, (1999).* Polyamines in Health and Nutrition" Rowett Research Institute, Aberdeen, United Kingdom, Publisher Springer New York, NY, Pages XIV, 336
7. *Bassiri H, Benavides A, Haber M, Gilmour SK, Norris MD, Hogarty MD (2015).* Translational development of difluoromethylornithine (DFMO) for the treatment of neuroblastoma. Translational Pediatrics. 2015; 4(3): 226-238

8. *Boiko GV, Mitchell MF, Hu W, Pangey DK, Mathevet P., et al. (1998).* Epidermal Growth Factor Receptor Expression in Cervical Intraepithelial Neoplasia and Its Modulation During an α-Difluoro-methylornitine Chemoprevention Trail. Clinical Cancer Research. 1998; 4: 1383-1391

9. *Büyükuslu N (2015).* Dietary Polyamines And Diseases: Reducing Polyamine Intake Can Be Beneficial In Cancer Treatment, Journal of Nutrients, 2015, 2(2): 27-38

10. *Büyükuslu N, Hizli H, Esin K, Garipagaoglu M (2014).* A Cross-Sectional Study: Nutritional Polyamines in Frequently Consumed Foods of the Turkish Population. Foods, 3(4), 541–557. doi:10.3390/foods3040541

11. *Cipolla BG, Guilli F, Moulinoux J-P.(2003).* Polyamine reduced diet in metastatic hormone-refractory prostate cancer (HRPC) patients. Biochem Soc Trans. 2003; Vol. 31, part 2: 384-387

12. *Cipolla BG, Havouis R, Moulinoux J-P(2010).* Polyamine reduced diet (PRD) nutrition therapy in hormone refractory prostate cancer patients. , 64(5), 0–368. doi:10.1016/j.biopha.2009.09.022

13. *Cipolla BG, Havouis R, Moulinoux JP. (2007).* Polyamine contents in current food: a basis for polyamine reduced diet and a study of its long-term observation and tolerance in prostate carcinoma patients. Amino Acid. 2007; 33: 203-212

14. *Deloyer P., Peulen O., Dandrifosse G. (2001).* Dietary polyamines and non-neoplastic growth and disease. European Journal of Gastroenterology & Hepatology, 13(9), 1027–1032. doi:10.1097/00042737-200109000-00005

15. *Devens BH, Weeks RS, Burns MR, Carson CL, Brawer MK. (2000).* Polyamine depletion therapy in prostate cancer. Prostate Cancer and Prostatic Diseases. 2000; 3: 275-279

16. *Dunzendorfer U, Russel DH. (1978).* Altered polyamine profiles in prosthatic hyperplasia and in kidney tumors. Cancer Res. 1978; 24: 519-524

17. *Fernández C, Sharrard RM, Talbot M, Reed BD, Monks N. (1995).* Evaluation of the significance of polyamines and their oxidases in the aetiology of human cervical carcinoma. British Journal of Carce. 1995; 72(5): 1194-1199. doi:10.1038/bjc.1995.485

18. *Feuer EJ, Merrill RM, Hankey BF. (1995).* Cancer surveillance series: interpreting trends in prostate cancer – part II: Cause of death misclassification and the recent rise and fall in prostate cancer mortality. J Natl Cancer Inst. 1999; 91: 1025-1032

19. *Fletcher S, Neill WA, Norval M. (1991).* Seminal polyamines as agents of cervical carcinoma: Production of aneuploidy in squamous epithelium. J Clin Pathol. 1991; 44: 410-415

20. *Fulton DS, Marton LJ, Lubich WP, Wilson CB (1982).* Polyamine levels in CSF from patients with pituitary tumors or nonneoplastic pituitary disease. Arch Neurol. 1982; 39(1): 47-48

21. *Garewal H, Sampliner R, Gerner E, Steibronn K, Alberts D, Kendall D. (1988).* Ornithine decarboxylase activity in Barrett's esophagus: a potential marker for dysplasia. Gastroenterology. 1988; 94: 819-821

22. *Garnica A, Benton T, Slanina P, Miale T, Stenke AL (1982).* Changes in urine polyamines in childhood leukemias. Ann Clin Lab Sci. 1981; 11(2): 109-114

23. *Gilmour SK (2007).* Polyamines and nonmelanoma skin cancer. Toxicology and Applied Pharmacology 224 (2007) 249–256 , doi:10.1016/j.taap.2006.11.023

24. *Horn Y, Beal SL, Walach N, Lubich WP., et al. (1982)* Further Evidence for the Use of Polyamines as Biochemical Markers for Malignant Tumors. Cncer Res. 1982; 42(8): 3248-3251

25. *Jakes R, Spillantini MG, Goedert M. (1994).* Identification of two distinct synucleins from human brain. FEBS Lett. 1994; 345: 27-32

26. *Jänne J, Pösö H, Raina A. (1978).* Poliamines in rapid growth and cancer. Biochim Biophys Acta. 1978; 473: 241-293

27. *Jensen JR, Lynch G, Baudry M. (1987).* Polyamines stimulate mitochondrial calcium

transport in rat brain. J Neurochem. 1987; 48: 765-772

28. *Jeon JH, Choi KH, Cho SY, Kim CW, Shin DM, Kwon JC. (2003).* Transglutaminase 2 inhibits Rb binding of human papillomavirus E 7 by incorporating polyamine. The EMBO Journal. 2003; 19: 5273-5282
29. *Kim YT, Yoon BS, Kim GW, Kim SH, Kwan GY, Kim GH. (2005).* Pretreatment levels of serum squamous cell carcinoma antigen and urine polyamines in woman with squamous cell carcinoma of the cervix. International Journal of Gynecology and Obstetrics. 2005; 91: 47-52
30. *Kingsnorth AN, Lumsden AB, Wallace HM. (1994b).* Polyamines in colorectal cancer. Br J Surg. 1994b; 71: 791-794
31. *Kingsnorth AN, Wallace HM, Bundred NJ, Dixon JM. (1994a).* Polyamines in breast cancer. Br J Surg. 1994a; 71: 352-356
32. *Kuniyasu S, Yoshihiko K, Masako S, Koichi T, Alan L, Fumio K (2009).* Long-Term Oral Polyamine Intake Increases Blood Polyamine Concentrations. Journal of Nutritional Science and Vitaminology, 55(4), 361–366. doi:10.3177/jnsv.55.361
33. *Kuniyasu S., Yoshihiko K. & Fumihiro C., (2012)* Food Polyamine and Cardiovascular Disease -An Epidemiological Study, Global Journal of Health Science, Vol. 4, No. 6; 2012; doi:10.5539/gjhs.v4n6p170
34. *Laukaitis CM, Gerner EW. (2011).* DFMO: Targeted risk reduction therapy for colorectal neoplasia. Best Practice and Resaerch Clinical Gastroenterology. 2011; 25: 495-506
35. *Lawton FG, Griffin M, Slack JA, Blackledge G. (1990).* Predicting response to chemotherapy for patients with epithelial ovarian cancer using urinary polyamine excretion patterns. Br J Cancer. 1990; 62(4): 692-694
36. *Lipton A, Sheehan L, Harvey HA. (1975)* Urinary polyamine levels in patients with gastrointestinal malignancy. Cancer. 1975; 36(6): 2351-2354
37. *Liu R, Bi K, Jia Y, Wang Q, Yin R, Li Q. (2012).* Determination of polyamines in human plasma by high-performance liquid chromatography coupled with Q-TOF mass spectrometry. Journal of Mass Spectrometry. 2012; 47(10): 1341-1346
38. *Luk GD, Baylin SB. (1983).* Ornithine decarboxylase as a biologic marker in familiar colonic polyposis. N Engl J Med. 1983; 311: 80-83
39. *Metcalf BW, Bey P, Danzin C, Jung MJ, Casara P, Vevert JP. (1978).* Catalytic irreversible inhibition of mammalian ornithine decarboxylase (EC4.1.1.17) by substrate and product analogues. J Am Chem Soc. 1998; 100: 2551-2553
40. *Meyskens FL, Gerner EW. (1999).* Development of difluoromethylornithine (DFMO) as a chemoprevention agent. Clin. Cancer Res. 1999; 5: 945-951
41. *Mitchell MF, Tortolero-Luna G, Lee GG, Hittelman WN, Lotan R., et al. (1998).* Phase I Dose De-escalation Trail of α-Difluoromethylornitine in Patients with Grade 3 Cervical Intraepithelial Neoplasia. Clinical Cancer Research. 1998; 4: 303-310
42. *Moulinoux J-Ph, Quemener V, Chambon Y (1987).* Evolution of red blood cell polyamine levels in partially hepatectomized rat. European Journal of Cancer and Clinical Oncology, 23(2), 237–244. doi:10.1016/0277-5379(87)90020-4
43. *Moulinoux JPh, Quemener V, Khan NA, Delcros JG, Havouis R. et al., (1989a).* Spermidine uptake by erythrocytes from normal and Lewis lung carcinoma grafted mice I. In vitro study. Anticancer Res. 1989a; 9: 1063-1068
44. *Moulinoux JPh, Quemener V, Khan NA, Havouis R, Martin C. (1989b.)* Spermidine uptake by erythrocytes from normal and Lewis lung carcinoma grafted mice II. In vitro study. Anticancer Res. 1989b; 9:1057-1062
45. *Moulinoux JPh, Quemener V, Larzul JJ, Le Calve M, Roch AM., et al. (1984a).* RBC polyamines in mice bearing the Lewis lung carcinoma (3LL) and in patients with bronchopulmonary cancers. Int J Cancer. 1984a; 34: 277-281
46. *Moulinoux J-Ph, Quemener V, Le Calve M, Chatel M, Darcel F. (1984b).* Polyamine in brain tumor; a correlative study between tumor,

spinal fluid and red blood cell free polyamine levels. J Neuro-Oncol. 1984b; 2: 153-158

47. *Muñoz-Esparza, Nelly C., Latorre-Moratalla, M. Luz, Comas-Basté, Oriol, Toro-Funes, Natalia, Veciana-Nogués, M. Teresa, Vidal-Carou, M. Carmen (2019)*. Polyamines in Food. Frontiers in Nutrition, 6(), 108–. doi:10.3389/fnut.2019.00108

48. *Nishibori N, Fujihara S, Akatuki T. (2006).* Amounts of polyamines in food in Japan and intake by Japanese Food Chem. 2006; 100: 491-497

49. *Nowotarski SL, Feith DJ, and Shantz LM (2015).* Skin Carcinogenesis Studies Using Mouse Models with Altered Polyamines, Cancer Growth and Metastasis, Cancer Growth and MetastasisVolume 8s1, https://doi.org/10.4137/CGM.S21219

50. *Okamoto A, Sugi E, Koizumi Y, Yanagida F, Udaka, S (1997).* Polyamine Content of Ordinary Foodstuffs and Various Fermented Foods. Bioscience, Biotechnology and Biochemistry, 61(9), 1582–1584. doi:10.1271/bbb.61.1582

51. *Osswald, H., Herrmann, R., Jones, G.R.N. et al. (1998)*. Urinary polyamine excretion by tumor-bearing and tumor-free mice exposed to cyclophosphamide, 5-fluorouracil and 6-mercaptopurine. J Cancer Res Clin Oncol 111, 141–148 (1986). https://doi.org/10.1007/BF00400753

52. *Phan N., Thanh B., Kuniyasu S., Masanobu K., (2011).* Mediterranean diet and polyamine intake: possible contribution of increased polyamine intake to inhibition of age-associated disease, Nutrition and Dietary Supplements 2011:3 1–7; DOI: 10.2147/NDS.S15349

53. *Quemener V, Khan NA, Moulinoux JPh. (1990).* Polyamines and cancer. Cancer J. 1990; 3: 45-52

54. *Quemener V. (1990).* Implications des polyamines dans le processus prolifératifs malins. D.Sc. Thesis in Pharmacy. University of Rennes, France. 1990.

55. *Ralph A., Englyst K., Bardócz S.(1999).* Polyamine content of the human diet. p.123-137 In boock "Polyamines in Health and Nutrition"edityd by Bardócz S. and White A, Rowett Research Institute, Aberdeen, United Kingdom, Publisher Springer New York, NY, Pages XIV, 336

56. *Rudman D, Kutner MH, Chawla RK, Goldsmith MA, Blackston RD, Bain R. (1979).* Serum and urine polyamines in normal and in short children. J Clin Invest. 1979; 64(6): 1661-1668

57. *Russel DH, Durie BG, Salmon SE, Lancet J. (1975).* Polyamines as predictors of success and failure in cancer chemotherapy. J Cancer. 1975; 25: 797-799

58. *Russel DH, Durie BG. (1978).* Polyamines as Biochemical Markers of Normal and Malignant Growth: Progress in Cancer Research and Therapy. Volume 8, Raven Press, New York. 1978; 139-155

59. *Russel DH, Gullino PM, Marton LJ., et al. (1974).* Polyamines depletion of the MTW9 mammary tumor and subsequent elevation of spermidine in the sera of tumor-bearing rats as a biochemical marker of tumor regression. Cancer Res. 1974; 34(9): 2378-2381

60. *Russel DH. (1977).* Clinical relevance of polyamines as biochemical marker of tumor kinetics. Clin Chem. 1977; 23(1): 22-27

61. *Sarhan S, Knödgen B, Seiler N. (1989).* The Gastrointestinal tract as polyamine source for tumor growth. Anticancer Res. 1989; 9: 215-224

62. *Saydjari R, Townsend CM, Barranco SC, Thompson JC. (1989).* Polyamines in gastrointestinal cancer. Dig Dis Sci. 1989; 34(10): 1629-1636

63. *Seiler N (2003).* Thirty Years of Polyamine-Related Approaches to Cancer Therapy. Retrospect and Prospect. Part 1. Selective Enzyme Inhibitors. Current Drug Targets, 4(7), 537–564. doi:10.2174/1389450033490885

64. *Seiler N, Delcros JG, Moulinoux JP. (1990).* Polyamine transport in mammalian cells. An update. Int J Biochem Cell Biol. 1990; 1(6): 591-596

65. *Shrestha RD, Fujimoto HS, Okui K (1992)* A Novel Anticancer Treatment for Xenoplanted Human Gastric Cancer Using Polyamine Antimetabolites in a Low Polyamine Diet The Japanese journal of Surgery (1992) 22:137-142

66. *Simoneau AR, Gerner EW, McLaren CE, Meyskens Jr. (2003).* Alpha-Difluoromethylornitine and Polyamine Levels in the Human Prostate; Results of a Phase II a Trail Journal of the National Cancer Institute. 2003; 93(1): 57-59

67. *Stanek J, Frei J, Mett H, Schneider P, Regenass U. (1992).* 2-Substituted, 3-(aminooxy) prop-anamines as inhibitors of ornithine decarboxylase: synthesis and biological activity. J Med Chem. 1992; 35: 1339-1344

68. *Thyss A, Milano G, Caldani C, Lesbats G, Schneider M, Lalanne CM. (1982).* Polyamines as biological markers in malignant lymphomas. Eur J Cancer Clin Oncol. 1982; 18(7): 611-616

69. *Uehara N, Kita K, Shirakava S. (1990a).* Elevated polyamine content in erythrocytes of malignant lymphoma patients. J Cancer. 1980; 71: 393

70. *Uehara N, Shirakawa S, Uchino H, Saeki Y. (1990b).* Elevated contents of spermidine and spermine in the erythrocytes of cancer patients. Cancer. 1980; 45(1): 108-111

71. *Verma AK. (1990).* Inhibition of tumor promotion by DL-alpha-difluoromethylornithine, a specific irreversible inhibitor of ornithine decarboxylase. Basic life sci. 1990; 52: 195-204

72. *Volkov N, Goldman SS, Flamm ES, Craioto H, Wolf AP, Brodie J. (1983).* Labelled putrescine as a probe in brain tumors. Science. 1983; 221: 673-675

73. *Wallace HM, Fraser AV, Hughes A. A (2003).* A perspective of polyamine metabolism. Biochem J. 2003; 376: 1-14

74. *Wallace HM. (2009).* The polyamines: past, present and future. Essays Biochem. 2009; 46: 1-9

75. *Zoumas-Morse C, Rock CL, Quintana EL, Neuhouser ML, Gerner EW, Meyskens FM. (2007).* Development of a Polyamine Database for Assessing Dietary Intake. J Am Diet Assoc. 2007; 107: 1024-1027

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