

## Evaluation of Anti-Blastoma Effects of Some Bacterial Vaccine in Combination with Chemotherapy

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### ABSTRACT

The present work discusses methods of goal-directed immune-correction and immune-rehabilitation of oncological patients using specific bacterial polyvalent vaccines. With this purpose the tetra-vaccine (Staphylococcus-Proteus-Clebsiella-Escherichia) has been used. Experiments have been carried out on white rats and mice with the use of three tumoral strains - Sarcoma-45, Sarcoma M-1 and Ehrlich's ascitic tumor. For chemotherapy of malignant tumors the following remedies were used: Cyclophosphan, Vincristin and Adriablastin. The vaccine and chemotherapy were applied in both ways, separately (control), and in combination. The results of investigations have shown that the best effect was achieved in case of combination of vaccine with chemotherapy - malignant tumors completely underwent regression, while using only tetra-vaccine, the percent of malignant tumor growth inhibition constituted only 37,6%. Thus, the received results are quite encouraging and the above-suggested method could be used for treatment of oncological patients.

**KEYWORDS:** cancer, vaccination, chemotherapy, bacterial vaccine

Nowadays in modern oncology the problem concerning improvements of immediate or delayed effects of treatment acquires an increasing importance. It is well known and recognized that surgical, medicament and radiation therapy results in various degree of immunodeficiency. The mentioned problem is especially important in patients with generalized cancer growth accompanied with marked disorders in immune system.

In oncological clinics for treatment of malignant tumor growth with various locations the new preparations and treatment schemes have been suggested. Due to dose limitation the radio- and chemotherapy in most cases is difficult, less effective and often accompanied with side effects (cardio-, nephro-, neuro- and hepatotoxicity and myelo-depressive effects of preparations). On the background of leukopenia and agranulocytosis the lethal outcome in case of intercurrent infections is high. Any measure taken in order to reduce such kind of complications would be the great success in treatment of oncological patients [2].

Application of bacterial polysaccharides has the dual mining in oncology: stimulation of specific antibacterial immunity (reduction of hospital infections) and increase in nonspecific resistance (improvement of immediate or delayed results of treatment) [4]. The analogues preparations of previous generation were suggested only for increasing of nonspecific resistance. They were distinguished by high toxicity and thereby useless for treatment. In modern oncology there are many immune preparations received from microbes of various taxonomic groups, but their use with dual effects (anti-microbial and anti-blastoma) has not been detected [3].

Such kind of works have been carried out in USA (Feller I., et al 1974) and Japan (Homma I.J., 1971) - vaccine of Pseudomona; in Germany (Oberling F. et. al., 1975) - complex di-vaccine; for anti-tumor purposes the antigen of Proteus was used (Antopol W., Shrisanthou C., 1972; Jamazak M., et. al., 1974); anatoxin of Staphylococcus (Ray P., et.al., 1982; Gordon R., et.al. 1983; Klausner et.al., 1985) [1], in Georgia (Zarkua Z., 1988) - di-vaccine of anatoxins of Proteus and Staphylococcus, for investigation of anti-blastomic effects. The above-listed

scientists stated the anti-bacterial and anti-blastoma effects of approved preparations.

During the latest 6 years investigation of anti-blastoma effects of bacterial vaccines have been carried out in laboratory and vivarium of chemical cancerogenesis at Oncology National Center. Has been studied the anti-blastomic, preventive and therapeutical effects of T-independent vaccine of Proteus, cleansed anatoxin of Staphylococcus, complex di-vaccine of Staphylococcus-Proteus, tetra-vaccine of Staphylococcus-Proteus-Escherichia-Clebsiella and corresponding hyper-immune plasmas.

### MATERIAL AND METHODS

Experiments have been carried out on white rats (body weight 100-120 g.) and mice (3-3,5 month, body weight - 18-20 g.) using Ehrlich's adenocarcinoma (EAT, ascitic type), sarcoma M-1 and S-45. Each animal had individual report card and were kept in the same feeding and caring conditions. Ehrlich's adenocarcinoma in mice was inoculated intraperitoneally; M-1 and S-45 in rats were inoculated subcutaneously in sub-scapular region.

Anti-cancerogenetic effects were evaluated by the rate of inhibition of malignant tumor growth and duration of life span. Received data were analyzed statistically.

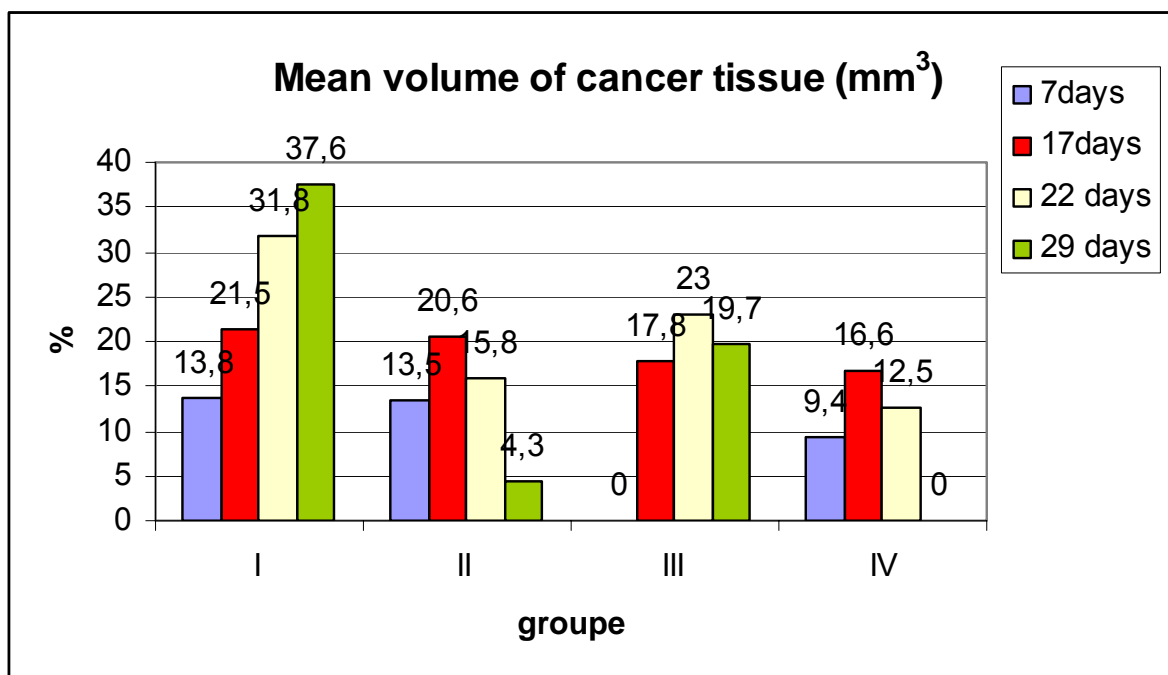
### RESULTS AND DISCUSSION

In experiment we have studied adjuvant effect of anti-carcinogenic mono-therapeutical effect of pure tetravaccine and in complex with chemotherapy. Of 4 groups, first was control, and rest 3 - basic (experimental). Animals underwent two course of chemotherapy (intraperitoneal injections of Adriablastin 50 mg/m<sup>2</sup>, Vincristin 2 mg/m<sup>2</sup>, Cyclophosphanum 200 mg/m<sup>2</sup>) on 17th and 25th days after inoculation (II and IV groups). Intra-peritoneal vaccinations were performed on 2nd, 5th, 8th and 11th days after cancer inoculation (II and IV groups) (Tab.1).

In the II experimental group the malignant tumor growth was sharply inhibited and delayed while in IV group the cancer tissue completely underwent resorption. The percentage of duration of life span was high as well.

Groups	Mean weight of animals			
	7 <sup>th</sup> day	17 <sup>th</sup> day	22 <sup>nd</sup> day	29 <sup>th</sup> day
Control Sa-45	20 135 g 13,8 mm <sup>3</sup> - -	- 21,5 mm <sup>3</sup> -	- 31,8 mm <sup>3</sup> -	117 g 37,6 mm <sup>3</sup> 27,8 day
Sa-45+chemotherapy 17-25 day	20 135 g 13,5 mm <sup>3</sup> 2,1% -	- 20,6 mm <sup>3</sup> 4,1 % -	- 15,8 mm <sup>3</sup> 52,8 % (6 resist.)	116 g 4,3 mm <sup>3</sup> 84,2 % 35,6 day (28%)
Sa-45+ tetra vaccine 2-5-8-11 day	20 136 g 8,3 mm <sup>3</sup> 39,8% -	- 17,8 mm <sup>3</sup> 17,2% (3 undeveloped)	- 23 mm <sup>3</sup> 27,6% (3 resist.)	140 g 19,7 mm <sup>3</sup> 37,6 % 39,8 day (43,4%)(4 resist.)
Sa-45+( tetra vaccine + chemotherapy) tetra vaccine 2-5-8-11 day chemotherapy 17-25 day	20 140 g 9,4 mm <sup>3</sup> 31,8% -	- 16,6 mm <sup>3</sup> 22,7% (4 undeveloped.)	- 12,5 mm <sup>3</sup> 60,7% (10 resist..)	148 g - 100% 43 day (54,6%)

**Tab.1** Results of the investigations.



**Fig.1** Changes of cancer tissue's mean volume in dynamics.

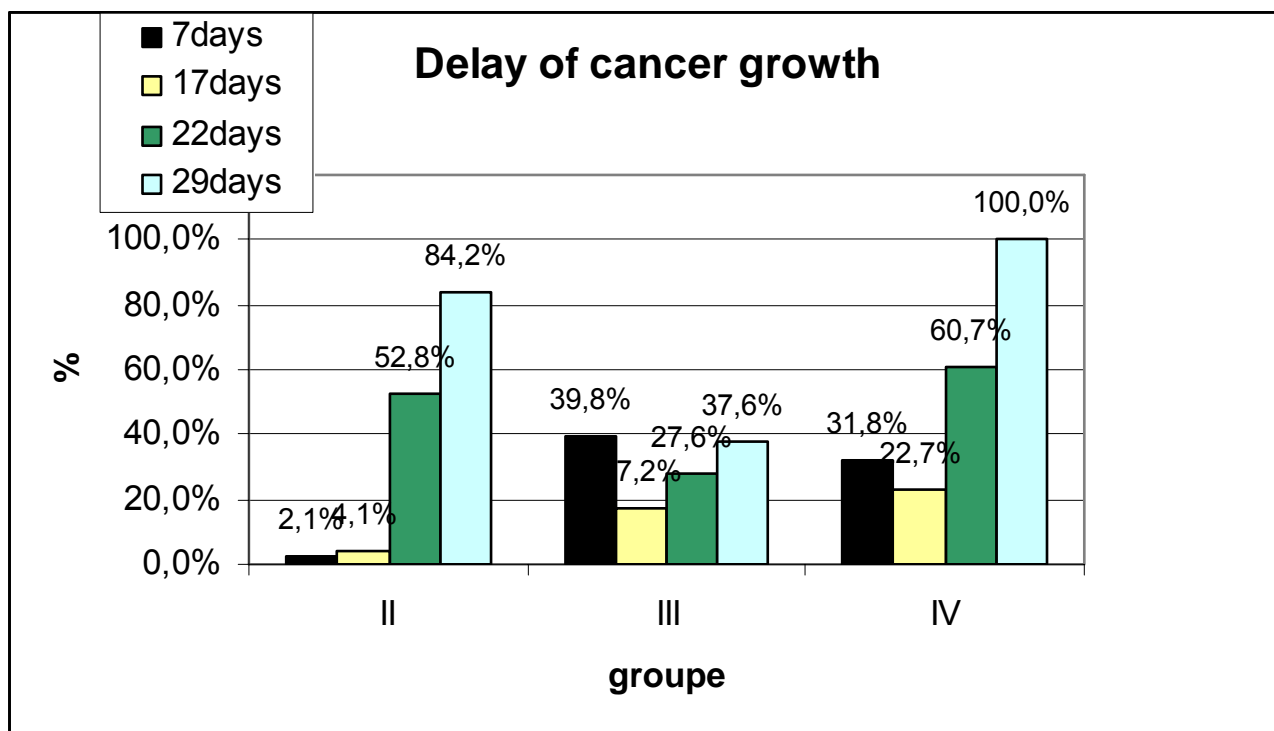
The best effect was revealed in the group IV as previously, where tetra-vaccine was used in combination with chemotherapy as adjuvant immune preparation.

**CONCLUSION**

Thus, it could be concluded that goal-directed immune correction and complete immune-rehabilitation of oncological patients is of great importance. The bacterial

immune-saccharides are able to increase specific antibacterial immunity and nonspecific resistance as well. All of the afore-said was confirmed and proved in our experiments. Bacterial vaccines have well expressed

mono immune-therapeutical and in complex with chemotherapy - positive adjuvant effect as anti-blastomas.



**Fig.2** Delay percent of malignant tumor growth.

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## Изучение антибластомных свойств некоторых бактериальных вакцин в комбинации с химиотерапией

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### РЕЗЮМЕ

Работа касается целенаправленной иммунокоррекции и иммунореабилитации больных с использованием специфических бактериальных поливалентных вакцин. С этой целью нами использована стафилококк-протей-клебсиелла-эшерихиозная тетравакцина. Эксперименты проведены на беспородных крысах и мышях с использованием трех опухолевых штаммов: саркома-45, саркома М-1 и асцитной опухоли Эрлиха. Исследования проводились методами, широко используемыми в экспериментальной химиотерапии опухолей. В качестве химиопрепаратов применяли: циклофосфан, винкристин и адриавластин. Вакцина и химиопрепараты применялись как в отдельности (контроль), так и сочетанно. Установлено, что наилучший эффект получен при сочетании с химиопрепаратами - опухоли полностью регрессировали. При использовании только тетравакцины процент торможения роста опухоли составлял 37,6 %. Полученные результаты весьма обнадеживают и метод рекомендуется для лечения онкологических больных.

**Ключевые слова:** рак, прививка, химиотерапия, противобактериальная вакцина